25 years / ans

WINNIPEG

CONFERENCE
CAHR 2016

25th Annual Canadian Conference on HIV/AIDS Research

May 12-15, 2016
Winnipeg, Manitoba

CONGRÈS DE
L'ACRV 2016

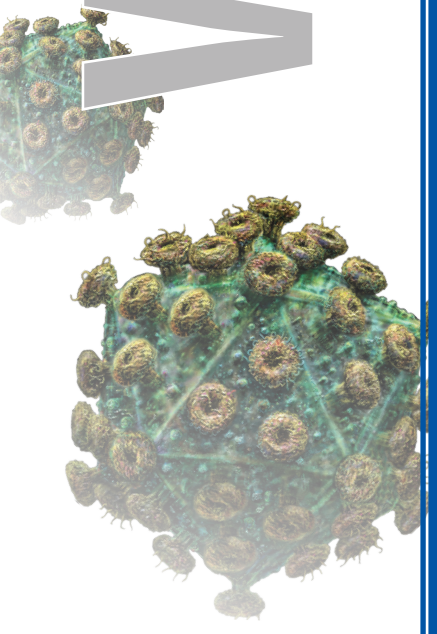
25e Congrès annuel canadien de recherche sur le VIH/sida

Du 12 au 15 mai 2016
Winnipeg (Manitoba)

Realizing Our Potential: Local to Global and Back

Réaliser notre potentiel : Du local au mondial et retour

ABSTRACTS
ABRÉGÉS



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

CAHR 2016

Realizing Our Potential: Local to Global and Back
25th Annual Canadian Conference on HIV/AIDS Research

ACRV 2016

Réaliser notre potentiel : Du local au mondial et retour
25e Congrès annuel canadien de recherche sur le VIH/sida

Abstracts / Abrégés

May 12 - 15, 2016 / 12 au 15 mai 2016

Winnipeg, Manitoba

Notice:
As you my have noticed, the abstracts of the 25th Annual Canadian Conference on HIV/AIDS Research (CAHR 2016) are not published in a scientific journal. CAHR extends its apologies for this inconvenience. CAHR had a long-standing relationship with the Canadian Journal of Infectious Diseases & Medical Microbiology (CJIDMM) to publish the abstracts of the annual CAHR Conference. However, in December 2015, the CJIDMM was sold and the new publisher informed CAHR in January 2016 that the journal would no longer publish the Conference abstracts. A search was taken to find a new journal in which to publish the conference abstracts, however there was not sufficient time to negotiate a new arrangement for CAHR 2016.

Avis :
Vous aurez sans doute remarqué que les abrégés du 25e Congrès annuel canadien de recherche sur le VIH/sida (ACRV 2016) ne sont pas publiés dans une revue scientifique. L'ACRV s'excuse de cet inconvénient. L'ACRV avait établi une relation avec le Journal canadien des maladies infectieuses et de la microbiologie médicale (JCMIMM) qui publiait les abrégés du Congrès annuel de l'ACRV. Toutefois, en décembre 2015, le JCMIMM a été vendu à un nouvel éditeur, qui a informé l'ACRV en janvier 2016 que le journal ne publierait plus les abrégés du congrès. Nous avons entrepris des recherches pour trouver une nouvelle revue dans laquelle publier les abrégés du congrès, mais nous n'avons pas eu suffisamment de temps pour négocier un nouvel accord pour l'ACRV 2016.

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

Twenty-five years ago, the 1st Annual Canadian Conference on HIV/AIDS Research was held in Montreal. As continues to this day, the event was hosted by the newly created Canadian Association for HIV Research. Today, the tradition continues with the Conference having been held in every time zone, from Victoria to St. John's, over the last three decades.

So much has changed over the last quarter century. Logistically, what started out as a small annual gathering of scientists is now the meeting place for 800-900 Conference goers, made up of researchers from all pillars of research, affected community members, students, policy makers, international delegates, and other interested parties. On the community front, the face of the epidemic has kept changing, severely impinging on the lives of different, mostly marginalized, populations. And on the research front, there have been many advances that have made inroads in tackling the disease – from insights into the biomedical complexities of the virus, to the development of advanced clinical approaches to treat HIV, to new and diverse strategies to reduce risks for individuals and communities.

While so much has changed, the relevance of CAHR and its annual Conference is a strong as it was some 25 years ago. For example, thousands of new infections occur each year in Canada, and the number of people living with HIV in Canada is rising. The Public Health Agency of Canada estimates that 70,000 people in Canada were living with HIV at the end of 2011, and there are over 3,000 new infections each year. Globally, more than 36.9 million people – the equivalent of the population of Canada – were living with HIV in 2014, according to the World Health Organization.

While so much has been achieved, there is clearly so much more to be done. As we look ahead, CAHR will continue to stay relevant, relying on what has become a hallmark of the association: its members' enthusiasm, shared commitment, and great willingness to learn from each other. We hope you enjoy CAHR 2016 and find it a worthwhile learning experience.

Dr. Michael Grant

Il y a vingt-cinq ans avait lieu à Montréal le premier Congrès annuel canadien de recherche sur le VIH/sida. Tout comme maintenant, l'événement était organisé par l'Association canadienne de recherche sur le VIH, qui venait tout juste de naître. De nos jours, la tradition se poursuit et le Congrès a eu lieu dans tous les fuseaux horaires, de Victoria à St. John's, au long des trois dernières décennies.

Tant de choses ont changé au cours du dernier quart de siècle. Sur le plan logistique, ce qui était au départ une petite réunion annuelle de scientifiques est devenue un congrès rassemblant de 800 à 900 congressistes, composé de chercheurs de tous les piliers de la recherche, de membres des collectivités touchées, d'étudiants, de responsables de l'élaboration des politiques, de délégués étrangers et d'autres parties intéressées. Sur le front communautaire, le visage de l'épidémie n'a cessé de changer, affectant gravement la vie de populations différentes, surtout marginalisées. Par ailleurs, sur le front de la recherche, de nombreux progrès sont intervenus, effectuant des percées vers la victoire contre la maladie, de découvertes sur les complexités biomédicales du virus à l'élaboration d'approches cliniques de pointe pour traiter le VIH et jusqu'aux diverses stratégies nouvelles visant à réduire les risques pour les personnes et les collectivités.

Même si beaucoup de choses ont changé, la pertinence de l'ACRV et de son Congrès annuel demeure d'actualité, tout autant qu'il y a 25 ans. À titre d'exemple, on recense chaque année au Canada des milliers d'infections nouvelles et le nombre de personnes vivant avec le VIH dans notre pays augmente. Selon l'Agence de la santé publique du Canada, 70 000 personnes au pays vivaient avec le VIH à la fin de 2011 et plus de 3 000 nouvelles infections sont recensées chaque année. Globalement, au-delà de 36,9 millions de personnes, soit l'équivalent de la population du Canada, vivaient avec le VIH en 2014, selon la statistique de l'Organisation mondiale de la santé.

Même si nous avons beaucoup accompli, il est évident qu'il reste beaucoup plus à faire. En regardant vers l'avenir, l'ACRV conservera sa pertinence, comptant sur ce qui est devenu la marque de l'association, soit l'enthousiasme, l'engagement commun et l'immense volonté de ses membres d'apprendre les uns des autres. Nous espérons que vous apprécierez tous les instants de l'ACRV 2016 et que vous y trouverez de précieuses expériences d'apprentissage.

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

We are pleased to welcome you to Winnipeg and congratulate CAHR on its 25th Annual Canadian Conference on HIV/AIDS Research. For a quarter century Canadian researchers have been making a difference in preventing new HIV infections, improving treatment and outcomes for those living with HIV and working to create a supportive, stigma-free and respectful environment for all persons at risk of infected with HIV. The annual CAHR conference is where we come together to share our challenges, successes, failures and next steps. While we can be proud of the progress we've made, everyone will agree that there is much more that needs to be accomplished toward our global goal of ending the HIV epidemic.

Toward that goal, the theme of this year's conference is "Realizing Our Potential: Local to Global and Back", and it highlights the leadership that Canadian researchers and their partners have played across Canada, and globally, to address the challenges we face in combatting the HIV epidemic. To make our goal of eliminating HIV a reality we must act locally, wherever local is, and share our lessons learned with the global community as we also learn from them. HIV/AIDS remains a significant challenge and a collective approach is required if we are to hasten our progress toward HIV elimination.

With the largest number of abstracts ever submitted to a CAHR conference, 504, it is clear that there is a great deal of enthusiasm and momentum in the Canadian HIV research scene. This has resulted in a scientific program with tremendous breadth as well as depth. To further foster interdisciplinary collaboration, we've created four concurrent multidisciplinary sessions. Our goal is that by sitting in a single session, you will be able to hear how a particular topic is being approached from all pillars of our research endeavour.

We'd like to thank all those who have made this year's conference possible, especially our Scientific Program Committee and the Conference Management Committee. We hope that you find this year's conference informative and engaging, that you connect with old friends and make new ones and that you even have a little bit fun.

Dr. Marissa Becker and Dr. Keith Fowke

C'est avec plaisir que nous vous accueillons à Winnipeg et que nous adressons nos félicitations à l'ACRV pour son 25e Congrès annuel canadien de recherche sur le VIH/sida. Depuis un quart de siècle, les chercheurs canadiens font la différence dans la prévention des nouvelles infections au VIH, améliorant les traitements et les résultats pour les personnes vivant avec le VIH et œuvrant afin de créer un environnement soutenant, respectueux et sans stigmates pour toutes les personnes à risque de contracter une infection au VIH. Le Congrès annuel de l'ACRV est l'endroit où nous nous rassemblons pour partager nos difficultés, nos succès, nos échecs et réfléchir sur les prochaines étapes. Nous pouvons être fiers des progrès accomplis, mais tous conviendront qu'il reste beaucoup plus à faire pour atteindre notre but global, éradiquer l'épidémie de VIH.

À cette fin, le thème du congrès de cette année est « Réaliser notre potentiel : Du local au mondial et retour », qui fait ressortir le leadership des chercheurs canadiens et de leurs partenaires au Canada et à l'échelle mondiale pour relever les défis auxquels nous faisons face pour lutter contre l'épidémie de VIH. Pour que notre objectif d'éliminer le VIH devienne réalité, nous devons agir au niveau local, quel que soit l'endroit que désigne le mot « local », et partager les leçons que nous avons retenues avec la collectivité mondiale, car nous apprenons également des chercheurs de tous les autres pays. Le VIH/sida demeure un défi de taille et il faut une approche collective si nous voulons accélérer les progrès vers l'élimination du VIH.

Cette année est celle du plus grand nombre d'abrégés jamais présentés à un congrès de l'ACRV, soit 504; il est évident qu'il y a beaucoup d'enthousiasme et d'animation sur la scène canadienne de la recherche sur le VIH. Cela a donné un programme scientifique d'une largeur et d'une profondeur exceptionnelles. Afin de stimuler encore plus la collaboration interdisciplinaire, nous avons mis au point quatre séances multidisciplinaires simultanées. Notre objectif est que, en assistant à une seule séance, vous serez à même de voir de quelle façon tel thème particulier est abordé par tous les paliers de notre entreprise de recherche.

Nous aimerions remercier tous ceux qui ont rendu possible le congrès de cette année, notamment notre comité du programme scientifique et le comité de gestion du congrès. Nous espérons que vous trouverez le congrès de cette année enrichissant et mobilisant, que vous reprendrez contact avec d'anciens amis et vous en ferez de nouveaux et que, même, vous aurez un peu de plaisir.

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Volet A : Sciences fondamentales

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Volet D : Sciences sociales

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Oral Presentations – Exposés oraux

Basic Sciences: Prevention

Sciences fondamentales : Prévention

BS1.1

Defining the role of the vaginal microbiome in mucosal vulnerability to HIV infection: Sialidase production by Gardnerella vaginalis subgroups

John J. Schellenberg[1], Teenus Paramel Jayaprakash[1], Niradha Withana Gamage[1], Mo H. Patterson[1], Mario Vaneechoutte[2], Janet E. Hill[1]

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Increased abundance of *Gardnerella vaginalis* and sialidase activity in vaginal fluid is associated with bacterial vaginosis (BV), which in turn is associated with increased risk of HIV infection in numerous studies worldwide. Sialidase, produced by some but not all *G. vaginalis* strains, cleaves terminal sialic acid residues from mucosal glycoproteins, including protective mucins, antibodies and surface molecules of antigen-presenting cells, leading to increased mucosal vulnerability and abrogation of immune effectors. Since most women are colonized with *G. vaginalis,* its status as a normal member of the vaginal microbiota or pathogen causing BV remains controversial. Numerous molecular techniques have been described in order to account for well-known phenotypic and phylogenetic diversity of *G. vaginalis* strains, while sequencing of the chaperonin-60 universal target (*cpn*60 UT) has clearly distinguished four subgroups in isolate collections, clone libraries and deep sequencing datasets since 2005. To clarify the potential clinical significance of *G. vaginalis* subgroups, we characterized 112 isolates from three locations (Canada, Belgium and Kenya). Isolates did not cluster geographically, with clearly differentiated intra- and inter-subgroup distributions of pairwise identity comparisons, indicating ancient divergence of subgroups. A gene encoding a putative sialidase was detected in all subgroup B (N=33), C (N=35) and D (N=8) isolates and in one of 36 subgroup A isolates. In contrast, sialidase activity as measured using a quantitative fluorometric assay was observed in all subgroup B isolates, only three subgroup C isolates (9%) and no subgroup A or D isolates. These observations indicate that *G. vaginalis* should no longer be considered a single entity, but rather as four species with potentially different roles in mucosal colonization, proliferation and biofilm formation. Genome sequencing, proteome profiling and epithelial cell co-culture are ongoing to better define the role of these important members of the vaginal microbiota in BV and increased vulnerability to HIV infection.

BS1.2

Comparison of three NRTI backbones Kivexa, Combivir, and Truvada, in a mouse pregnancy model

Kayode Balogun, Nicole Banko, Eszter Papp, Jeffrey Lu, Hakimeh Mohammadi, Lena Serghides

Toronto General Research Institute, University Health Network, Toronto, ON

Nucleoside reverse transcriptase inhibitors (NRTIs) are the key backbone of the current combination antiretroviral therapy (cART) used to prevent mother-to-child transmission of HIV. The use of cART during pregnancy has been associated with adverse birth outcomes that could be due in part to the mitochondrial toxicity of NRTIs. Direct comparison of the effect of available NRTI regimens on pregnancy outcomes is lacking. We investigated the effects of *in utero* exposure to three well-known NRTI backbones (Kivexa, Combivir, and Truvada) on placental mitochondrial toxicity and fetal outcomes using a mouse pregnancy model.

Female C57BL/6 mice were exposed to human-relevant plasma concentrations of Combivir (AZT/3TC), Kivexa (abacavir/3TC), Truvada (emtricitabine/tenofovir), or water (control) starting from gestational day (GD) 1 through to 15. At GD 15 fetuses and placentas were collected, and birth outcomes were assessed by fetal weight, viability and resorption; obvious morphological differences in the fetuses were also recorded. The placental gene expression of the key enzymes involved in mitochondrial function, oxidative stress, and biogenesis were analyzed using qPCR.

Truvada caused lower fetal resorption and higher fetal weight compared to Combivir and Kivexa. We observed a number of fetuses with morphological defects in the Combivir group. There was a significant increase in the placental expression of the mitochondrial specific enzymes, DNA polymerase gamma (Polg), and MnSOD, in mice exposed to Truvada, which correlated positively with the gene expression of cytochrome c oxidase subunit 2. The expression of citrate synthase, a commonly used maker of intact mitochondria was also significantly upregulated in the placentas of mice on Truvada compared to other NRTIs.

Our data suggest that Kivexa, Combivir, and Truvada exhibit different toxic effects on the placenta. Truvada was associated with the best fetal outcomes. Further investigation of these NRTI backbones in combination with additional antiretrovirals (as part of cART) are currently underway.

BS1.3

The Effect of E157Q in HIV-1 Integrase on R263K-Mediated Dolutegravir Resistance

Kaitlin Anstett[1, 2], Vincent Cutillas[1, 2], Robert Fusco[3], Thibault Mesplede[1], Mark A. Wainberg[1, 2]

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Background: The integrase strand transfer inhibitor (INSTI) dolutegravir (DTG) has a high genetic barrier to resistance, which has only been selected in treatment-experienced patients and in tissue culture. The novel R263K substitution in integrase is the predominant mechanism of DTG resistance in INSTI-naïve patients. However in INSTI-experienced patients, resistance emerges through the accumulation of resistance substitutions for other drugs of this class. E157Q can be selected after treatment with raltegravir (RAL), and is a polymorphism present in the circulating virus as well. As it was recently reported that a patient failed RAL and subsequently DTG with the E157Q substitution, we investigated the effects of this substitution on the emergence of R263K, its effects on enzyme biochemical function, and viral infectivity and drug resistance.

Results: R263K decreased integrase strand transfer, DNA binding activities, and NL4.3 infectivity by ~20% when compared to WT. Neither biochemical function nor infectivity showed a significant decrease from WT when the E157Q mutant was evaluated, and the presence of this substitution in the R263K background partially restored the enzymatic and infectious defects conferred by the latter mutation. While the E157Q mutant was hyper-sensitive to DTG, the double mutant displayed a 10-fold increase in DTG resistance compared to R263K alone.

Conclusions: DTG is arguably one of the best current therapies for HIV infection, displaying a high genetic barrier for resistance and very few treatment failures to date. However, we show that the E157Q substitution is able to restore the defects in enzyme function and viral infectivity that are conferred by the DTG resistance mutation R263K. As position 157 in IN is polymorphic, its presence at the initiation of DTG therapy is possible, which could lead to the selection of a replicatively competent, DTG-resistant virus. This could have important consequences for the clinical care of HIV-positive individuals.

BS1.4

Pre-clinical evaluation of the therapeutic application of a vaccine targeting the 12 protease cleavage sites

Ma Luo[1, 2], David Tang[1], Jorge Pinto[3], Mikaela Nykoluk[1], Philip Lacap[1], Jeffrey Tuff[1], Elnaz Shadabi[2], Chris Czarnecki[1], James Whitney[4], Maria Alonso[3], Terry B. Ball[1], Gary Kobinger[5], Paul Sandstrom[1], Francis A. Plummer[5]

1. National HIV and Retrovirology Laboratory, JC Wilt Infectious Diseases Research Centre, National Microbiology Laboratory, Winnipeg, MB 2. Department of Medical Microbiology, University of Manitoba, Winnipeg, MB 3. University of Santiago de Compostela, Santiago de Compostela, Spain, 4. BIDMC, Harvard Medical School, Boston, MA, USA, 5. National Microbiology Laboratory, Winnipeg, MB

Background: Effective therapeutic vaccines used in combination of ARV to treat HIV infected patients can reduce drug induced toxicity, help to re-constitute immune system and achieve a functional cure. We conducted a pilot study to test the therapeutic effect of a novel HIV vaccine targeting the 12 protease cleavage sites in combination of ARV.

Methods: SIVmac251 infected rhesus monkeys were treated with a combination of FTC, PMPA and raltegravir for 49 days. Seven days after ARV initiation the monkeys in the treatment group received rVSVpcs (i.m.). Three additional therapeutic treatment with rVSVpcs (i.m.)/NANOpcs(i.m.), NANOpcs(i.m), and NANOpcs(i.m.) were carried out with 2-week intervals. ARV treatment was stopped after 49 days and plasma viral load and proviral load, CD4/CD8 counts, antibody and T cell response to PCS peptides and non-PCS Gag and Env peptides were analyzed.

Results: ARV treatment suppressed viral load of all macaques, but only the viral load of 6 out of 11 macaques was suppressed to non-detectable level during the treatment/ARV period. However, even with the short duration of ARV treatment and incomplete viral load suppression, the immune responses to PCS peptides were generated after 4 therapeutic treatments. The CD4 counts of PCS vaccine treated macaques were significantly improved after 35 days and 49 days of ARV treatment($p=0.027$ and 0.044), whereas there is no significant improvement in CD4 counts of monkeys only received ARV treatment despite the viral load suppression.

Conclusions: Our study showed that new immune response to PCS peptides can be generated even with incomplete viral load suppression after a short period ARV treatment. The combination of PCS vaccine treatment and ARV generated new immune response to PCS peptides, improved CD4 counts of SIVmac251 infected monkeys and can be used to improve patient care to achieve a functional cure.

BS1.5

Tracing HIV's Footsteps; Dissemination of HIV-1 following Intra-vaginal Infection in a Humanized Mouse Model

Jocelyn M. Wessels[1], Philip V. Nguyen[1], Kristen Mueller[1], Varun Anipindi[1], Fatemah Vahedi[1], Uladzimir Karniychuk[1], Marianne Chew[1], Alexandre Deshiere[2], Tony Mazzulli[3], Michel J. Tremblay[2], Ali A. Ashkar[1], Charu Kaushic[1]

1. McMaster University, Hamilton, ON 2. Universite Laval, Quebec City, QC 3. Mount Sinai Hospital, Toronto, ON

Humanized mouse (Hu-mice) models are an increasingly valuable tool for HIV research. While simian models of heterosexual HIV transmission suggest an initial vaginal infection that disseminates to other tissues, a comprehensive analysis of viral distribution and infection kinetics is noticeably lacking for Hu-mice. NOD/Rag2/gamma c -/- mice reconstituted with CD34+ hematopoietic stem cells were systemically (intra-peritoneal IP) or mucosally (intra-vaginal IVAG) infected. Plasma viral titres quantified by a clinically validated real-time PCR were significantly higher ($P<0.05$) in IP infected mice ($1.9x10^5 \pm 4.2x10^4$ RNA copies/mL) compared to IVAG ($6.3x10^4 \pm 8.8x10^3$). Following IVAG infection, an abundance of HIV-1 was detected in vaginal washes 1 week post-infection ($3.2x10^6 \pm 1.9x10^6$) which decreased over 5 weeks ($1.1x10^5 \pm 4.2x10^4$). Significant depletion of CD45+CD4+ cells was seen by flow cytometry in the blood of infected Hu-mice between week 0 and 5 (42.6±9.3% vs. 1.6±0.7%; P=0.01) while control animals remained unchanged (28.7%±7.9% vs. 13.0±10.6%; P=0.3). Additionally, CD3+ T cell depletion was seen in the vaginal mucosa of infected Hu-mice but not uninfected controls using immunohistochemistry. While the vaginal viral load declined between week 1-5, the plasma titre significantly increased from week 1 ($6.3x10^3 \pm 3.8x10^3$) to 5 ($2.2x10^5 \pm 7.2x10^4$; P=0.007). Using p24 as a proxy marker of infection, we identified CD45+p24+ cells in the vaginal mucosa, spleen and blood at 1 and 5 weeks post-infection by flow cytometry. To identify extent of dissemination, tissue homogenates were prepared and HIV copies/mL were quantified by PCR. Initial results showed the greatest number of copies ($>1x10^7$) present in vagina, uterus, bone marrow, spleen, and lung followed by liver, colon, kidney, heart, brain, skeletal muscle, bladder, rectum, and small intestine. Overall, results show that following intravaginal inoculation HIV establishes a local infection which is followed by rapid systemic dissemination to all tissues in Hu-mice. These results are in agreement with the proposed model of heterosexual HIV transmission in women.

BS1.6

Next generation sequencing reveals the temporal complexity of mixed hepatitis C infections among people who inject drugs in Vancouver, BC, Canada

Jeffrey B. Joy[1], Weiyan Dong[1], Don R. Kirkby[1], Jason Grebely[2], Richard H. Liang[1], Vera Tai[1], Anita Howe[1], P. Richard Harrigan[1], Art F. Poon[1]

1. BC CFE HIV/AIDS, Vancouver, BC 2. University of New South Wales, Sydney, NSW, Australia

Background: Direct acting antiviral (DAA) therapies targeting the hepatitis C virus (HCV) have radically changed HCV treatment. The performance of direct acting antiviral (DAA) therapies in individuals with mixed HCV infections (infection with 2 or more distinct viral variants) remains unclear. Sanger and some next-generation sequencing (NGS) methods do not have the resolution to detect minority genotypes. In this study we sought to investigate the presence and temporal dynamics of mixed infections among people who inject drugs (PWID).

Methods: We used Sanger sequencing and stored plasma samples collected between 1997 and 2007 from 121 HCV seroconverting, treatment-naïve PWID. Each sample sequenced was also HLA-typed to confirm database annotations on source individuals. Four follow-up samples were obtained from candidate mixed infections. All samples for each candidate mixed infection were further sequenced using Sanger, whole-genome, and random-primer methods on an Illumina MiSeq NGS platform. Resulting data was subsequently processed using a custom bioinformatic pipeline.

Results: Sanger sequencing revealed a remarkably complex pattern of changes in HCV variants within individual patients between time points. 18 patients (15%) displayed 20 changes (2 patients changed twice) in HCV variant over time. 9 patients displayed 9 changes between variants of HCV GT1a; 9 patients displayed 11 changes between genotypes/subtypes (7 GT3a-GT1a, 3 GT1a-GT3a, and 1 GT1b-GT1a). HLA typing revealed only one mislabeled sample (subsequently excluded), showing that laboratory errors do not account for our results**.** NGS with random primers revealed that 10 infections were concurrently composed of multiple genotypes, with dynamic cycling of these genotypes occurring within individuals between time points.

Conclusion: Current DAA therapies are often genotype- and subtype-specific. Treatment of dominant genotypes may allow expansion of minority genotypes. A quantitative understanding of the variation present in infected patients will likely become crucial, particularly in high-risk populations such as PWID or HIV/HCV co-infected patients.

Clinical Sciences: Clinical Care

Sciences cliniques : Soins cliniques

CS1.1

Weekly text-messaging (Weltel) to engage vulnerable HIV+ populations: It works, what does it cost?

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Background: In certain settings, mobile health (text messaging) interventions improve antiretroviral (ART) adherence and HIV viral load (VL) suppression in HIV+ patients. However, little data exists on effectiveness in vulnerable North American populations, or on real world cost and time required to enable such an intervention.

Methods: We conducted an effectiveness study using the WelTel model with 85 participants on ART at Oak Tree Clinic, Vancouver, Canada. Inclusion criteria included age ≥14 years, prescribed ART, detectable HIV VL (>200 copies/mL), and "vulnerable" (i.e. ≥1 of: unstable housing, active addiction, domestic violence, poor care engagement/adherence, advanced HIV infection/AIDS, or mental health factors). Cell phones with unlimited texting were given to participants if needed and all then received a weekly interactive text message check-in for one year. A clinic nurse triaged and managed responses, logging interactions by type, health care providers (HCPs) involved, and time usage. Demographic, clinical and adherence data were collected for pre-intervention and intervention years. Repeated measures mixed-effects linear regression assessed CD4 count and VL (log_{10} transformed), while logistic regression assessed ART adherence and appointment attendance from pre-intervention to intervention years.

Results: Mean ART adherence improved from 61.7% to 68.3% (p<0.0001), and median population HIV log_{10}VL declined by 0.70 log (p=0.007) from pre-intervention to intervention years. Median VL decline for responders (response rate ≥50%) was 1.03 log (vs. 0.39 log, p=0.03), and adherence increase 13.7% (vs. 0.8%, p=0.008) versus non-responders (response rate <50%). Managing "problem" responses required 53 minutes of HCP time/participant/year, for a cost/patient of $45.20. Total intervention cost (including phones, plans, staff time) was $375.74/patient/year.

Conclusions: Text messaging is an effective tool for improving ART adherence and VL in especially vulnerable HIV+ patients. Weekly patient contact does not significantly increase clinic work load, and carries a modest cost/patient for those most vulnerable to morbidity and death.

CS1.2

Incidence of emergent drug resistance mutations during clinical use of integrase inhibitor-containing antiretroviral regimens in British Columbia

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Background: In British Columbia (BC), integrase inhibitor (INI) use in antiretroviral therapy (ART) and prevalence of INI resistance are both increasing. This observational study examines the incidence of drug resistance mutations in a BC cohort of INI-treated patients.

Methods: HIV-1-infected persons age ≥19 years were included if their first prescription for raltegravir, elvitegravir or dolutegravir was dispensed 01-Jan-2012 to 31-Dec-2014 through the BC Centre for Excellence in HIV/AIDS (BC-CfE) drug treatment program, and were followed until death, loss-to-follow-up, last viral load (VL) or 31-Oct-2015. Those without baseline drug resistance testing or VL monitoring during follow-up were excluded.

Clinical variables and drug resistance tests were abstracted from BC-CfE databases. Emergent INI or other (reverse transcriptase, protease) resistance was defined as new mutations conferring intermediate-high level resistance to ≥1 INI or other antiretroviral (score ≥30 Stanford HIV drug resistance algorithm v7.0.1). Incidence rates for resistance were calculated per 1000 person-years. Patient characteristics and outcomes were summarized by descriptive statistics.

Results: 1217 persons contributed 1322 distinct INI-patient records. Background ART, baseline VL suppression and treatment experience varied between groups. Emergent INI, INI plus other, or other (no INI) resistance occurred with raltegravir 4, 7, 10, total 21/480 (4.4%), elvitegravir 1, 3, 3, total 7/367 (1.9%) and dolutegravir 1, 2, 2 total 5/475 (1.1%) respectively in ART-naïve and experienced patients (see Table for rates, mutations). Recently marketed INIs had shorter follow-up to date, with less opportunity for emergent resistance.

Conclusion: Emergent resistance was observed with all INIs, but resistance rates were low. Follow-up continues.

Table: Baseline characteristics and outcomes of integrase inhibitor-treated persons

Baseline characteristics			
1st yr INI available in study period	**2012**	**2013**	**2014**
Age median (Q1-Q3) yr	50 (42-55)	43 (34-51)	49 (40-55)
Sex n(%) male	384 (80)	270 (74)	382 (80)
Baseline VL <50 copies/mL n(%)	254 (53)	160 (44)	309 (65)
ART naïve n(%)	67 (14)	77 (21)	68 (14)
ART co-prescribed with INI:			
2 NRTI: tenofovir + 3TC or FTC	166 (34)	320 (87)	102 (21)
2 NRTI: abacavir+ 3TC	101 (21)	0 (0)	277 (58)
Other ART combination	213 (44)	47 (13)	96 (20)
INI exposure and virologic outcomes			
Treatment duration, INI regimen:			
Cumulative drug exposure, person-yr	703	393	444
Follow-up, median (Q1-Q3) yr	1.6 (0.9-2.5)	1.2 (0.8-1.7)	1.0 (0.8-1.2)
Virologic suppression n(%):			
Suppressed, VL <50c/mL	279 (58)	225 (61)	338 (71)
Not suppressed, no drug resistance	180 (38)	135 (37)	132 (28)
Not suppressed, emergent drug resistance	21 (4)	7 (2)	5 (1)
Incidence of emergent intermediate to high level drug resistance mutations			
Any resistance/ 1000 person-yr (CI95)	29.9 (18.5-45.7)	17.8 (7.2-36.7)	11.3 (3.7-26.3)
Time to any resistance, median (Q1-Q3) yr	0.7 (0.3-1.2)	0.9 (0.3-1.1)	0.5 (0.4-0.7)
INI resistance/ 1000 person-yr (CI95)	15.4 (7.7-27.6)	10.2 (2.8-26.0)	6.8 (1.4-19.7)
Emergent INI resistance mutations			
(number of cases)	66A (1)		
138A/E (1)			
140A/S+148H/R (4)			
143C/H/R/Y (2)			
155H/N (5)			
163G/I/R/V (2)	66I (1)		
92Q (1)			
145S (1)			
147G (1)	66I (1)		
263K (2)			
Other resistance/ 1000 person-yr (CI95)	24.1 (14.0-38.8)	15.3 (5.6-33.2)	9.0 (2.5-23.1)
Emergent other resistance mutations			
(number of cases)	184V/I (12)		
other NRTI (4)			
NNRTI (1)	184V/I (6)	184V/I (4)	
other NRTI (1)			

Definitions: **ART**: Antiretroviral therapy; **INI**: Integrase inhibitor; **NRTI**: Nucleoside(tide) reverse transcriptase inhibitor; 3TC: lamivudine, **FTC**: emtricitabine; **NNRTI**: Non-nucleoside reverse transcriptase inhibitor; person-yr: each person contributed cumulative drug exposure from start date to emergent resistance or censor date; **VL**: HIV plasma viral load; **Suppressed**: Achieved (<24 weeks) and/or maintained VL <50c/mL; **Not suppressed**: VL not <50 c/mL by 24 weeks and/or rebound (>200c/mL or ≥2 consecutive >50 c/mL). CI95: 95% confidence interval, Fisher's exact

CS1.3

Estradiol and Progesterone Levels Across Pregnancy in HIV-positive Women Randomized to Either Lopinavir/ritonavir or Efavirenz Based cART

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Background: Maternal cART during pregnancy is now recommended by most national and international guidelines. The near elimination of vertical HIV transmission by cART has been one of the greatest successes of the HIV epidemic. However cART use during pregnancy has been associated with higher rates of adverse birth outcomes such as low birth weight (LBW), small for gestational age (SGA) birth, preterm delivery (PTD), and stillbirth. The mechanisms that underlie these adverse events are poorly understood. We have previously shown that levels of progesterone were lower in Canadian HIV+ women on protease inhibitor (PI)-based cART compared to uninfected controls. Here we examine progesterone and estradiol levels across pregnancy in a previously completed Ugandan cohort of HIV+ women randomized to receive either PI-based (lopinavir/ritonavir) or NNRTI-based (efavirenz) cART.

Methods: Women were recruited between gestational week (GW) 16-28. Blood samples were collect at 4-week intervals. 157 women from the efavirenz arm and 165 women from the lopinavir/ritonavir arm were included in this study. Rates of adverse pregnancy outcomes did not differ between arms (previously published). Hormones levels were assessed by ELISA. A linear-mixed-effect model was used to examine longitudinal changes in hormones by treatment arm. Wilcoxon rank-sum test was used to examine associations between hormones and birth outcomes.

Results: Estradiol was higher across pregnancy in women receiving lopinavir/ritonavir compared to efavirenz

(p<0.0001). Progesterone did not differ between treatment arms. Estradiol levels were lower in women with SGA (p=0.0049 at GW24-28, p=0.04 at GW28-32), and LBW (p=0.013 at GW24-28, p=0.0021 at GW28-32) outcomes in the efavirenz-arm, but not in the lopinavir/ritonavir-arm. Levels of progesterone (at GW28-32, p=0.0057) and estradiol (at GW32-36, p=0.007) were lower in cases of stillbirth, and levels of both hormones declined immediately prior to stillbirth in 5 of 8 cases.

Conclusions: Lopinavir/ritonavir during pregnancy is associated with elevated estradiol levels.

CS1.4

Pregnancy Loss among Women Living with HIV and the Role of Antiretrovirals; a Canadian Perspective

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Background: The majority of Canadian women living with HIV (WLWH) are of reproductive age and more are reporting a desire to become pregnant following modern advances in HIV therapy. Although there are observed reductions in vertical transmission risk, some studies have suggested an increased incidence of adverse pregnancy outcomes (e.g. small-for-gestational-age, low birth weight and preterm birth) after exposure to antiretroviral therapy. This study seeks the link between reported antiretroviral use and pregnancy loss (stillbirths and/or miscarriages).

Materials & Methods: The association between antiretroviral exposure and pregnancy loss was analyzed using a sample of WLWH enrolled in the Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS), a longitudinal, community-based research study that enrolled 1425 WLWH in British Columbia, Ontario, and Quebec between 2013-2015. The outcome of interest was pregnancy outcome, defined as live birth, stillbirth or miscarriage. To capture this association, GEE modelling was utilized to consider correlation among multiple pregnancies from the same women. Demographics and pregnancy information were collected to adjust for potential confounding.

Results: A total of 2678 reported pregnancy outcomes were eligible for analysis, 2183 (82%) of which occurred prior to HIV diagnosis. Of the 495 pregnancies that occurred post-HIV diagnosis, 336 (68%) pregnancies were exposed to antiretovirals. HIV status and antiretroviral exposure during pregnancy were not significantly associated with pregnancy loss. However, the odds of having a pregnancy loss were significantly higher when antiretroviral therapy was initiated before conception (OR=3.59, 95% CI=1.253-10.289, P-value=0.002) compared to antiretroviral therapy initiated after conception. Ethnicity, previous pregnancy loss, maternal age during pregnancy, year of pregnancy, unplanned pregnancy and pregnancy location did not correlate with pregnancy loss in the post-HIV diagnosis and antiretroviral-exposed pregnancies that were analyzed.

Conclusions: The relationship between antiretroviral use, especially in the periconception period, and pregnancy loss requires further study.

CS1.5

Non-perinatal HIV acquisition among Canadian born pre-school children in Montreal, Quebec

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Background: While exceedingly rare, we have recently seen cases of non-perinatal HIV acquisition among Quebec-born children. The objective of this study was to determine the number, characteristics and risk factors for non-perinatal HIV acquisition among pre-school children in Montreal.

Methods: Medical charts at the two tertiary pediatric centers in Montreal (Montreal Children's Hospital and Sainte-Justine Hospital) were reviewed to identify all new cases of HIV infection among Quebec-born children between 2005-2015.

Results: Of 11 new pediatric HIV infections, 8 were perinatal transmissions, while in 3 cases mode of transmission is unknown. Case 1 was diagnosed after he presented with acute bacterial epiglottitis at age 4. Subsequent investigation of the family led to diagnosis of Case 2, his 5-year-old sibling. Both parents were HIV negative. Genetic testing confirmed that these were the biological parents of both children. Extensive investigations by psychologists, child protection services and public health, along with HIV phylogenetic analysis, failed to reveal the source of HIV. Case 3 was a 3 year-old born to an HIV positive mother, who had been determined to be HIV negative by several viral load tests in infancy, negative HIV DNA PCR, and seroreversion. At 36 months of age, she presented with bilateral parotitis and cervical adenopathy, and was subsequently diagnosed with acute HIV infection. While phylogenetic sequencing suggested similarity between her virus and that of her mother's, an extensive family investigation did not reveal a mode of transmission.

Conclusions: Nearly 30% of new HIV cases among Canadian-born children in the province of Quebec over the last decade were non-perinatally acquired, with no clear

mode of transmission determined in these cases. While these cases may simply represent an unusual situation, physicians should remain vigilant for signs of acute HIV infection in the absence of perinatal risk factors.

CS1.6

Infant Zidovudine prophylaxis for PMTCT: Is 4 weeks Enough? Data from the Canadian Perinatal HIV/AIDS Surveillance

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Background: While Canadian PMTCT guidelines still recommend 6 weeks of infant zidovudine (ZDV) prophylaxis, some HIV experts are prescribing 4 weeks only in low-risk situations. We interrogated the Canadian Perinatal HIV/AIDS Surveillance on duration of ZDV prophylaxis and infant outcomes.

Methods: A retrospective analysis of the CPHSP database reviewed outcomes of HIV-exposed infants who received only 4 weeks of ZDV. Inclusion criteria: infant born in Canada between 1997-2014, mother on cART in pregnancy, maternal VL<1000 copies/mL near delivery, infant prescribed ZDV mono-prophylaxis, ZDV duration available.

Results: 1252 infants met the inclusion criteria. Maternal VL near delivery was <50 copies/mL in 90% and 50-999 copies/mL in 10%. Infant ZDV duration was 6 weeks (39–45 days) in 87%, 4 weeks (25-31 days) in 7% and other durations in 6%. Among 82 infants stopping at 4 weeks, 74 (90%) were in BC, representing 26% of all BC infants during that time. Reasons for discontinuation were reported for 9 infants and included neutropenia (3), anemia (2), high lactate (1), parental decision (2), low risk infant (1). There were no cases of intrapartum/postnatal vertical transmission. There was one in utero transmission with documented maternal cART interruption and transiently detectable VL in the third trimester.

Conclusion: In the CPHSP, the majority of infants still receive 6 weeks of ZDV prophylaxis. Of those receiving 4 weeks, most are from a single site. In this cohort of well controlled MIPs, the single case of in utero transmission would not have been affected by infant ZDV duration. Although further study is necessary, these data suggest that a 4 week course of ZDV in very low risk situations is reasonable. Shortened duration lessens medication burden, risks of myelosuppression and could decrease longterm adverse effects.

Epidemiology and Public Health: HIV Prevention for Key Populations

Épidémiologie et santé publique : Prévention du VIH dans les populations clés

EPH1.1

High incidence of subsequent HIV seroconversion among Montreal PEP users

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Background: Patients consulting for post-exposure prophylaxis (PEP) are at great risk for contracting HIV. The aim of this study is to determine the incidence of HIV seroconversion after PEP use for sexual exposures.

Methods: All HIV-negative patients with ≥20weeks follow-up data post-PEP available were evaluated for HIV seroconversion. Person-time was calculated from PEP consult to the last negative or first positive HIV test. Backwards conditional Cox regression was used to estimate the factors associated with HIV seroconversion.

Results: 1350 patients were included. Patients were male (96%) and MSM (91%) with a mean age of 33 years (range 18-74y). 67% of patients had one PEP, while 33% had repeated PEP episodes. 200 patients (15%) had at least one syphilis infection during follow-up. 129 patients (10%) had also consulted for PrEP. Median follow-up was 176 weeks (IQR 91-273) representing 5075 person-years of follow-up. Eighty-nine (7%) patients seroconverted after PEP use for an HIV incidence rate of 1.75cases per 100 person-years (95% CI 1.43-2.16/100py). Patients with a high exposure risk at the time of the PEP consultation have an incidence rate 2.76 times greater than those with a low exposure risk (1.96 vs. 0.71 cases/100 py, respectively). All seroconverted patients were MSM with mean age of 33 years (range 21-51y). Younger patients (aHR=0.96; p=0.002), those with syphilis infection following PEP (aHR=4.55; p<0.001) and those who had a moderate to high exposure risk at their first PEP consult (aHR=2.40, p=0.04) were at greater risk of acquiring HIV following a PEP consultation. The number of PEP consults was not associated to HIV seroconversion (p=0.20).

Conclusions: Patients consulting for PEP are at high risk of acquiring HIV. Young, MSM individuals with a history of STIs and at-risk behavior are most vulnerable to HIV infection. Patients consulting for PEP should consider PrEP as an alternative therapy.

EPH1.2

High incidence of subsequent HIV seroconversion amongst MSM accessing recurrent non-occupational post-exposure prophylaxis (NPEP) in Vancouver, BC

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Identifying MSM who are at high risk for HIV seroconversion may allow for targeted combination prevention strategies.

We reviewed outcomes of individuals accessing the NPEP pilot program offered in Vancouver from July 2012 to December 2014. Data linkage with the Provincial Drug Treatment Program (DTP) was performed to determine subsequent seroconversion, defined using initiation of ART as a proxy measure . We calculated HIV incidence rates based on potential risk exposures from the date of first receipt of NPEP until June 30, 2015. Individuals not registered in the DTP database at this date were considered not to have seroconverted. We performed bivariate analyses of factors associated with seroconversion.

Over the study period, 559 unique individuals accessed the NPEP program (91% male, median age 33 [Q1-Q3: 27–41 years]) with 57 recurrent users. Overall 79% reported condomless anal intercourse (CAI) as their risk exposure for accessing NPEP. Ten individuals seroconverted; all were male, with a median age of 30 years (Q1-Q3: 27– 40 years) and median time to ART initiation from NPEP start of 25.4 weeks (Q1-Q3: 15.9–29.1 weeks). The incidence rate overall was 1.70/100 person-years (PYs): 2.24/100PYs for MSM, 2.30/100PYs for MSM reporting CAI, and 7.14/100PYs for those with >1 course of NPEP. In bivariate analysis comparing NPEP users who subsequently initiated ART vs. those who did not, we found no significant differences in time from exposure event to NPEP initiation (35 hours versus 22 hours, p=0.31), likelihood of completing 4 weeks of NPEP (67% versus 78%, p=0.87), or having a known HIV-positive partner (6% versus 35%, p=0.18).

Recurrent NPEP use identifies a sub-group of MSM at high risk of new HIV infection (incidence rate 7.14/100PYs). Additional prevention strategies including pre-exposure prophylaxis should be made available to these individuals.

EPH1.3

Understanding HIV Transmission among Persons from African, Caribbean and Black Communities in Canada: Comparison of those Infected Prior to and After Arrival

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Background: In 2014, people from HIV-endemic countries were 6-fold more likely to be diagnosed with HIV than other Canadians. It is currently unknown what proportion acquired HIV pre- or post-arrival in Canada nor whether there are differences in risk factors.

Objective: The MSAFIRI Study aims to characterize HIV acquisition in African, Caribbean and Black (ACB) communities in Ontario.

Methods: Our multi-stage design involves (1) analysis of the OHTN Cohort Study (OCS), a multi-site clinical cohort of adults attending HIV care in Ontario, and (2) quantitative & qualitative interviews with HIV-positive ACB persons. We present results from Stage 1. We restricted the analysis to OCS participants born in sub-Saharan Africa, the Caribbean, or Canada. They were classified as born or infected since arriving in Canada, infected prior to arrival, and indeterminate; we report statistically significant differences ($p<0.0001$) in characteristics between these groups.

Results: Of 825 ACB participants, 46.9% were female. Among males, 49% reported sex with men (MSM). Participants attributed HIV infection to heterosexual exposure (72.0%), MSM (23.4%), MSM-IDU (2.7%), and IDU (1.9%). Birth regions were Canada (8.2%), the Caribbean (33%), Africa (53.7%), and elsewhere (5.1%). For 49.5%, we could not determine whether infection occurred pre- or post-arrival; for the remainder, 66.9% were infected pre-arrival and 33.1% were definitively infected after arrival. Those born in Canada or infected post-arrival were more likely to be male (71%), LGBQT (50%), and infected through MSM (43.5%), MSM-IDU (10.1%) or IDU (6.5%) exposure. Those infected prior to arrival were more likely to be female (62%), heterosexual (89.5%), and infected through heterosexual exposure (87.1%).

Conclusions: It is time to revisit assumptions about HIV transmission among ACB persons in Canada. Our prevention strategies should more closely reflect the evolving

epidemic. Results from Stage 2 will provide additional understanding of transmission contexts.

EPH1.4

Childhood Maltreatment, Protective Factors in Adolescence, and Sexual Risk Behaviour Among Homeless Youth: A Latent Class Analysis of Homeless Youth In Toronto

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Background: Homeless youth are an especially vulnerable population to poor psychosocial and wellbeing outcomes. It is currently unclear how previous maltreatment and current strengths and protective factors intersect for homeless youth, a group at high-risk for poor long-term outcomes such as addiction, criminal justice involvement, and sexual risk-taking.

Methods: Following a latent class analysis approach, we examined maltreatment and protective factor profiles of 251 homeless youth surveyed in Toronto. We used sexual, physical, and emotional abuse and neglect as measures of childhood maltreatment; social support, hopefulness, and resilience as measures of protective factors in adolescence; and involvement in sex work and condomless sex as measures of sexual risk-taking. We calculated the conditional probability of being in a class from standardized scores of the maltreatment and protective factors scales. We used *Entropy*, the Bayesian Information Criterion and the Lo-Mendel-Rubin likelihood ratio test to identify the best fit model.

Results: Our sample was primarily white, young (mean age=19.2) and male (60%). Fit indices suggested a three-class model best fit the data. Class I (*n*=106) reported a higher probability of social support, resilience, and hopefulness, but few abuse and neglect experiences. Class II (*n*=84) presented with multiple abuse and neglect experiences, but also resilience and hopefulness. Class III (*n*=61) presented with childhood abuse but no protective factors. Compared to Class I members, Class II members reported more lifetime sexual partners (RR=1.01, 95%CI: 1.01-1.02; p=0.04) and condomless sex (RR=1.98, 95%CI: 1.05-3.72; p=0.03) at last sexual intercourse.

Conclusions: Our findings suggest that homeless youth present with distinct patterns of maltreatment, protective factors, and sexual risk-taking. Treatment and interventions in homeless youth services should focus on fostering social support and resilience factors among youth who have experienced maltreatment in order to reduce HIV risk behaviors.

EPH1.5

HIV/STI sexual risk among transgender men who are gay, bisexual, or have sex with men: Trans PULSE Project

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Background: The World Health Organization has identified transgender (trans) men who have sex with men as a key population at disproportionate risk of sexually transmitted HIV. Yet in fact, there is a dearth of research evidence regarding HIV risk in this population. This study is among the first to examine factors associated with HIV/STI risk among trans men who are gay, bisexual, or who have sex with men (T-GBMSM).

Methods: In 2009-2010, 433 trans people in Ontario participated in a multi-mode respondent-driven sampling survey, including 158 T-GBMSM. Analyses were weighted using RDS II methods to adjust for differential recruitment probabilities; confidence intervals were adjusted for clustering by shared recruiter. Prevalence ratios (PR) for associations with past-year high sexual risk activity (condomless intercourse outside a seroconcordant, monogamous relationship) were estimated using average marginal predictions from logistic regression.

Results: Of T-GBMSM (mean age=29.8; 52% living full-time in felt gender; 25% Aboriginal or persons of colour; 0% self-reported HIV-positive), 10% had past-year high sexual risk. Among the 34% with a past-year cisgender male sex partner, this proportion was 29%. In multivariable analyses, older age, childhood sexual abuse (CSA; adjusted PR; APR=14.03, 95% CI=2.32, 84.70), living full-time in one's felt gender (APR=5.20, 95% CI=1.11, 24.33), and being primarily or exclusively attracted to men (APR=5.54, 95% CI=2.27, 13.54) were each associated with sexual risk. Indicating confounding and suggesting potential mediation, depression, stimulant use, and lack of parental support for gender identity predicted sexual risk only in the absence of control for childhood sexual abuse.

Conclusions: HIV prevention interventions targeting T-GBMSM who are predominantly attracted to men, or that address sequelae of CSA, may be warranted. Future HIV prevention research should examine the role of CSA in sexual risk for this group, and enroll larger samples of T-GBMSM who are sexually active with cisgender (non-trans) men.

EPH1.6

Sustained Reduction in Sexual Risk of HIV Transmission Following Diagnosis with Acute or Recent HIV Infection Among Gay Men in Vancouver, British Columbia

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Background: In prior interviews with gay men diagnosed with acute or recent HIV, men expressed concern about transmitting HIV to sexual partners and abstained from sex immediately following diagnosis, with resumption influenced by viral load and other factors. This study uses follow-up survey data to quantify how acute/recent diagnosis affected subsequent sexual behaviour.

Methods: In 2009-2012 we recruited newly diagnosed gay men with acute or recent HIV (latter based on testing negative in the previous year). Participants completed baseline and 5 follow-up questionnaires over 1 year including sexual network information on 5 recent partners (dyads). Primary outcomes were any anal sex (AS; with or without condoms) and condomless AS with a sero-discordant/unknown status partner (CAS-SDU). We used Kaplan-Meier survival curves and hierarchical generalized linear mixed effects models for each outcome (CAS-SDU using AS dyads only).

Results: The 25 participants reported 266 dyads (mean follow-up: 352 days). Most identified as gay (96%), Caucasian (64%), with college/university education (67%). Ten participants reported no partners in the first 3 months after diagnosis. Twenty-two (88%) participants reported ≥1 AS dyad after diagnosis. Median time to first AS was 80 days (IQR: 21-127). After considering/adjusting for relevant confounders (e.g., treatment, substance use, viral load), AS was significantly less likely in all time periods following diagnosis and more likely in dyads involving HIV-positive partners. Twelve (55%) reported ≥1 CAS-SDU dyad; median time to first CAS-SDU was 116 days (IQR: 24-302). The likelihood of CAS-SDU in AS dyads decreased following diagnosis and was higher in recent versus acute participants.

Conclusions: These findings confirm that most gay men in our study abstained from sex immediately after diagnosis with sustained longer-term reductions in both AS and CAS-SDU. Increasing timeliness of HIV diagnosis for gay men – particularly during acute infection – is a priority for reducing onward HIV transmission.

Social Sciences: Indigenous Health

Sciences sociales : Santé des Autochtones

SS1.1

"Condom in Grandma's Bag:" Experiences of Elders participating in an arts-based HIV/AIDS education workshop for Aboriginal youth

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Background: Little research has been done to explore the role Elders play and wish to play in HIV/AIDS education and prevention with Indigenous youth. This presentation explores how Elders attending an HIV/AIDS education workshop for youth experienced the workshop and how they perceive their roles in HIV/AIDS education and prevention.

Methods: 11 youth and 5 Elders representing the diverse groups of Aboriginal 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 Aboriginal youth. Participatory filmmaking was used to engage youth and create dialogue about HIV/AIDS, sexual health and health in general. 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: Preliminary findings include: the Elders found the participatory filmmaking process to be a positive experience; they felt comfortable discussing issues around HIV prevention with each other and with the youth in this environment; they found the workshop to be a valuable learning experience; relationships were built between the youth and Elders; the filmmaking process and the film itself helped the Elders identify their HIV/AIDS and sexual health learning needs; the Elders identified that they had a role to play in the education and support of youth in their community; the Elders identified their need for knowledge in order to educate and support youth.

Conclusion: These findings suggest that participatory filmmaking is a promising arts-based approach providing a good platform for creating constructive dialogue and engagement among youth and Elders in the context of HIV/AIDS education.

SS1.2

Refining the Research Response: An Aboriginal HIV Research Strategy

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Canadian Aboriginal AIDS Network, Ottawa, ON

Introduction: HIV remains an epidemic in Aboriginal communities in Canada with current outbreaks in the Prairie Provinces. Researchers and community members are seeking new evidence to inform strategic and effective responses to prevent new infections, eliminate stigma and discrimination and reduce AIDS-related deaths.

Goal: The goal of this project was to create and disseminate an Aboriginal community-led strategic research agenda in response to HIV & AIDS in the Aboriginal community.

Method: We used a three phased approach to this project including: 1) a comprehensive literature review to help us identity main themes; 2) face-to-face consultations with an inclusive range of stakeholders; and 3) an online questionnaire. Our data analysis was participatory, including several member checks, and grounded in community identified themes.

Results: We conducted 19 consultations with 172 Aboriginal people living with or affected by HIV, researchers, clinicians, service providers and Traditional Knowledge Keepers. An additional 40 individuals completed our online questionnaire. Results indicate that understanding and combatting racism, HIV-related stigma and discrimination remain top priorities for Aboriginal people living with and affected by HIV. These concerns are amplified for those in 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, poverty, housing, Hepatitis C, and other co-morbidities. A clear preference emerged, however, for research approaches to these issues are that Aboriginal-led, community-based, strengths-based and that build capacities in the community.

Conclusion: An Aboriginal community-led research strategy is not only desirable but a necessary step in our response to HIV and AIDS in Aboriginal communities. Funders, decision-makers and allied stakeholders would do well to support and be guided by this broad-reaching research strategy that is grounded in Aboriginal community concern.

SS1.3

The Cedar Project: Conducting Health Research in a Good Way

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As elected Chief of Splatsin Secwepemc Nation, I have been concerned about HIV and HCV epidemics among our young people and the need for meaningful, evidence-based research that addresses vulnerability within our communities in a culturally safe way. The Cedar Project is an ongoing cohort study addressing HIV and Hepatitis C vulnerability among more than 700 young Indigenous people who use drugs in Vancouver and Prince George, British Columbia. Since the study's inception in 2003, the Cedar Project Partnership, an independent body of Indigenous elders, leaders, scholars, and health/social service experts, has governed the entire research process, including ethics, study design, data interpretation and knowledge translation, ensuring voices of young at-risk Indigenous people are heard. The Partnership ensures: meaningful participation of young people; honouring participants' experiences; acknowledgement of the role of residential school and child welfare systems in health outcomes among Indigenous young people; and return of knowledge to Indigenous communities. Young Indigenous participants are protected by Partnership governance, and student trainees are taught how to conduct ethical and culturally-safe research involving Indigenous people. The Cedar Project model of research has been critical for us to conduct ground-breaking, culturally safe research that influences decision makers and informs evidence-based interventions. My aim is to discuss our approach to community governance, research activities, and knowledge translation/dissemination.

SS1.4

Housing and Health for Indigenous People Living with HIV in Canada: Preliminary Findings from the Stable Homes, Strong Families Community-Based Research Study

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Introduction: Although substantial research links housing and health for people living with HIV, less is known about what healthy housing means for Indigenous people living with HIV (IPHA). This knowledge is of critical importance given the disproportionate rates of HIV and higher rates of homelessness amongst Indigenous people in Canada. *Stable Homes, Strong Families* aimed to identify concepts of home for IPHAs, gaps in appropriate housing options and to facilitate the development of 'strengths-based' and culturally appropriate housing policies.

Methods: Drawing on decolonizing and Indigenous methodologies and principles of two-eyed seeing, data were collected through five 4-day Digital Storytelling workshops in Toronto (x2), Victoria, Regina and Fredericton. Nineteen participants (8 men, 10 women, and 1 trans) developed vis-

ual narratives that synthesized images, video, voiceovers, music, and text to create first-person reflections on home. Workshops were supported by local Elders and community-based organizations, peer and academic researchers. Traditional, localized ceremonies, teachings and sharing circles were integrated throughout. Our participatory analysis process drew upon our team's teachings to ground our analysis in Mohawk, Cree, Syilx Métis, Anishinaabe, and Haudenosaunee knowledge.

Findings: Several key themes emerged from our participatory analysis process of mapping key quotes from the digital stories onto a circular, wholistic representation of wellness: embodying home, home is a journey, home is necessary for managing health, and home as a relational and cultural experience. Meanings of home were connected to family, nature, culture and as a source of sacredness that resides within.

Conclusions: All digital stories included accounts about the importance of spirituality, teachings, family, and elders. Cultural knowledge, experience and practices were intertwined throughout. Findings help to clarify how housing practices and policies aimed at supporting IPHAs and those affected by HIV might be grounded in Indigenous culture.

SS1.5

Digging Deep: Examining the Root Causes of HIV and AIDS Among Aboriginal Women

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Aboriginal Women are over-represented in HIV/AIDS statistics, and the literature indicates that Aboriginal women, in particular, are the most marginalized population in Canada. Yet there is a startling lack of gender-specific (sex, lesbian, transgendered), Aboriginal-specific, HIV/AIDS resources, programs and services. . In this context, this research endeavours to contribute towards a deep understanding of the drivers that fuel this reality while identifying the assets within the Aboriginal community that sustain women and contribute to culturally relevant solutions to.

This research is important and timely given the multiple risk situations that contextual the daily lived experiences of many Aboriginal women. For Aboriginal people in Canada, colonization remains one of the most destructive elements affecting societal structures today. Our focus on Aboriginal women is to support them to develop evidence-based, community and asset-based solutions that are culturally safe. Our specific objectives include:

1. Understanding the complex Aboriginal social determinants of health that interact to produce higher rates of IDU, HIV/AIDS, and HCV among Aboriginal women, particularly those who are identified as hard to engage and those who have not been tested;
2. Developing a model of culturally safe care;
3. Increasing the research capacity of All Nations Hope Network (ANHN) –and the broader Aboriginal community in Regina (pilot site);
4. Developing educational videos to accompany the culturally safe care model and enhancing the understanding of cultural safety for Aboriginal women living with HIV, AIDS and HCV.
5. Our oral presentation will highlight a CIHR-funded, 3 year project that is community-based and employed Indigenous community-based research methods. An overview of our community research partnership will be provided as well as key points of the potential benefits to the community we serve and the health practitioners we work with and engage as we pursue positive systemic change. We will also provide time for questions and dialogue.

SS1.6

"What can lower HIV risk in the North is accepting you are LGBT": Exploring social drivers of HIV with Indigenous and Northern LGBT youth in the Northwest Territories

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Background: In the Northwest Territories (NWT) youth STI rates are 10 times Canada's average, which elevates HIV infection risk. Geographic isolation and stigma enhance HIV/STI vulnerability in the NWT. Stigma targeting lesbian, gay, bisexual and transgender (LGBT) youth is a social driver of HIV. Scant research has examined the lived experiences of LGBT youth in the NWT. We explored stigma and sexual health among LGBT youth in the NWT.

Methods: This community-based research project with Indigenous and LGBT community-based organizations in the NWT conducted in-depth interviews with LGBT youth (n=44) and key informants (n=30) in Yellowknife, Hay River, Fort Smith, Inuvik and Behchoko. Interviews were recorded and transcribed verbatim, and analyzed using narrative thematic techniques.

Results: Youth participants (mean age: 22.3 [SD: 4.5]; Indigenous: 16%; ethno-racial minority: 18%, cisgender women: 36%, cisgender men: 34%, transgender: 30%) identified as bisexual (30%), gay (30%), pansexual (16%), lesbian (11%), questioning (7%), and queer (7%). Key informants included Elders, Indigenous agency workers, nurses, social workers, and secondary school teachers. Narratives suggested pervasive stigma targeting LGBT youth exists across familial, educational, community, and healthcare settings. Stigma exacerbated Northern social isolation, increased depression and substance use—these factors elevated engagement in sexual risk practices. Narratives described a lack of safer sex knowledge tailored for LGBT

youth. Indigenous youth discussed racism in predominantly non-Indigenous LGBT communities, and the intersection of stigma with intergenerational trauma and colonization. Stigma was intensified in smaller communities. Protective factors included community-building and online support.

Conclusions: This is the first study to explore social drivers of HIV among Northern and Indigenous LGBT youth in the NWT. Syndemics of stigma, mental health and substance use converge to elevate exposure to HIV/STI. HIV prevention strategies tailored for LGBT youth in Northern Canada should address stigma, mental health, and racism, with attention to Indigenous youth's lived experiences.

Basic Sciences: Immunology

Sciences fondamentales : Immunologie

BS2.1

TLR10 is Significantly Increased in HIV-1 Infected Breast Milk Cells and Affects the Level of HIV Infection and Integration

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Toll-like receptors (TLRs) play a crucial role in innate immune recognition of pathogen-associated molecular patterns (PAMPs) and serve as part of the first line of defense against pathogen infection. Of the 10 human TLR family members, TLR10 remains an orphan receptor whose PAMPs and functions are poorly understood. In blinded studies, we found that breast milk cells isolated from HIV-1-infected women showed significantly increased expression of TLR1, TLR2 and TLR10 compared to uninfected milk cells. Indeed, TLR10 expression in HIV-infected milk cells was upregulated over 100-fold compared to uninfected milk cells. Further, we demonstrated that HIV-1 infection was significantly enhanced in reporter TZMbl cells transiently overexpressing TLR10 alone and coexpressing TLR2 or TLR1. Importantly, stably transformed TZMbl cells expressing TLR2 or TLR10 showed significantly increased HIV-1 integration, while proviral DNA was significantly decreased in cells treated with TLR10 siRNA prior to HIV-1 infection. Stimulation of breast milk cells *in vitro* with ssRNA40 or HIV-1 resulted in significantly increased TLR2 and TLR10 expression. Studies concerned with identification of PAMPs for TLR10 indicated that in MCF-10A mammary cells, TLR10 expression was significantly increased in response to Pam_3CSK_4 and gp41, while in THP-1 cells TLR10 was significantly increased in response to p17 and were readily knocked down with prior TLR2 and/or TLR10 siRNA treatment. Neutralization of TLR10 with anti-TLR10 antibodies significantly reduced IL-8 responses to HIV-1 p17, gp41 and Pam_3CSK_4 in THP-1 cells, and gp41 and Pam_3CSK_4 in MCF-10A cells. Breast milk cells *in vitro* highly responded to HIV-1 proteins p17, p24, gp41and Pam_3CSK_4 with increased NFκB activation. Lastly, siRNA knockdown of TLR10 decreased NFκB activation by p17 and gp41 in MCF-10A cells. Overall our results demonstrate for the first time that TLR10 appears to play an important role in HIV-1 infection, integration and innate immune responses.

BS2.2

DMPA Use Associates with Innate Immune Activation and Reduced Epithelium Repair Pathways in the Female Genital Tract

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Roughly 12 million sub-Saharan African women use injectable hormonal contraceptives with depot medroxyprogesterone acetate (DMPA) used most commonly. DMPA use is associated with a 2-fold increased risk of HIV acquisition; however the mechanism is not fully understood. Here, we report the first study to evaluate the effect of DMPA on mucosal surfaces in women at the molecular level to understand biological drivers of this observation.

Cervicovaginal secretions from 86 women, including DMPA (n=23) and non-hormonal contraceptive users (n=63), were analyzed using tandem-mass spectrometry. Data was evaluated using a combination of data-driven multivariate modeling and pathway analysis, adjusting for clinical and epidemiological variables.

Of the 487 unique proteins identified, 54 were found to be differentially abundant (adj. $p<0.0078$) between DMPA users and controls. Bleeding ($p=4.14E-4$) and necrosis of epithelial tissue ($p=4.45E-6$) pathways were activated, while specific immune response pathways (antigen presentation ($p=1.3E-5$) and phagocytosis ($p=5.2E-6$)) were inhibited among DMPA users. Further to this, our multivariate model (LASSO/PLSDA) uncovered a signature of 23 proteins that classified DMPA users from controls with 97% accuracy (92% CV, $p<0.0001$). This DMPA signature showed a relationship between increased epithelial breach and wounding signals (KRT16, KRT6A, SPRRF, TACSTD2), and an activation of an inflammatory response (IL36G, C1S, GC, HMGB1), with the reduction of mucosal repair (TFF3, CTSV, RBP4) and cornified envelope (SPINK5, CTSV) factors.

This signature may be indicative of a weakened genital epithelial barrier, with an increased likelihood of breaches and the corresponding inflammation processes. Based on these

findings, we hypothesize that the magnitude of epithelial wounding signatures and immunological impairment induced by DMPA, at the mucosal frontline and site of HIV exposure, are contributors to HIV acquisition risk, and should be validated in a prospective study. These molecular signatures may be useful to guide safe contraceptive formulations for women at high risk for HIV.

Study funded by CIHR TMI 168358.

BS2.3

Inducing immune quiescence with hydroxychloroquine as a new method to prevent HIV infection

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Introduction: HIV-exposed seronegative individuals (HESN) remain HIV uninfected despite being highly exposed to HIV. Our group has demonstrated this phenotype is associated with a reduced state of immune activation/inflammation called immune quiescence. Hydroxychloroquine (HCQ) is a non-steroid anti-inflammatory drug used to decrease inflammation in chronic diseases and has been shown in-vitro to suppress HIV replication. We hypothesize that the use of HCQ could decrease levels of inflammation thereby reducing the number of HIV target cells in the female genital tract.

Methods: Low-risk women from Kenya were enrolled in this study and followed for three months. At month 1, systemic/mucosal baseline immune activation was assessed. Participants received 200mg of HCQ daily and were followed for a 2 months period to assess change T cell immune activation (systemic and mucosal).

Results: Daily oral administration of HCQ decreases by 40% the frequency of HIV target cells at the systemic compartment (p=0.009). Furthermore, for those participants with confirmed HCQ levels at the FGT, we observed a significant decrease of HIV target cells (CCR5+CD4+) at the female genital tract (p=0.05).

Conclusion: The use of HCQ resulted in the induction of the Immune Quiescence phenotype both systemically and at the FGT. The use of anti-inflammatory agents to reduce immune activation/inflammation could represent a new approach to reducing HIV risk among certain groups.

BS2.4

Depletion of Memory and Tfh cells in Mesenteric Lymph Nodes of SIV-infected Rhesus Macaques

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Background: Celiac, superior and inferior Mesenteric lymph nodes (MLNs) drain the large and small intestine, and play a key role during the immune response. Studies have shown that MLNs are essential for tolerance to commensal bacteria and food antigens, but also represent major reservoirs for SIV in infected rhesus macaques. Although depletion of CD4 T cells in the intestinal lamina propria is a hallmark of Aids, the impact of SIV infection in MLNs is less known regarding the dynamics of CD4, T follicular helper (PD-$1^{high}$$CXCR5^{+}$), and B cells.

Methods: Rhesus macaques (RMs) were infected with SIVmac251. RMs were sacrificed at different time point post infection and MLNs were recovered. Tfh cells and CD4 T cell subsets were analyzed by flow cytometry. Because Tfh cells are essential for B cell maturation, we also investigated B cell dynamics.

Results: We demonstrated the progressive loss in the percentage of CD4 T cells in MLNs, which is associated with an increase in the percentage of CD8 T and B cells. However, total CD4 T cell numbers decrease only in RMs progressing fast to AIDS (FP). Hence, we show an early decline in both percentage and number of effector memory CD4 T and Tfh cells in FP. Interestingly, tissue memory B cell numbers increase in slow progressor animals (SP) consistent with the dynamics of Tfh cells.

Conclusion: Our results show for the first time a loss of Tfh and memory CD4 T cells in MLNs early after SIV infection, which is associated with the absence of B cell differentiation. This observation might be crucial regarding the role of immune system in controlling microbiota homeostasis.

This work was supported by the CIHR, the Canadian HIV Cure Enterprise (CanCURE), and the French National Agency for AIDS Research (ANRS) to JE. JE holds a Canada Research Chair.

BS2.5

Profile of B Cell Subsets and Vaccine Responses in HIV-Exposed Uninfected (HEU) Children

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Background: HEU children face a heightened incidence of morbidity and exhibit immunologic abnormalities, including higher frequencies of $CD19^+$ B cells, suggesting that exposure to HIV and/or antiretroviral agents (ARVs) could impact immune system development. We examined how heightened $CD19^+$ B cell frequencies were echoed in B cell phenotypic profiles, differentiation, and vaccine responses in HEU.

Methods: HEU (n=32) exposed to maternal ARVs in utero and combination ARV therapy from 12h after birth until week 6 were stratified based on peak maternal HIV viral load (VL) during pregnancy (<40 vs ≥40 copies/ml). Mononuclear cells were isolated from cord blood (CB) and from peripheral blood at 6 months of age. Flow cytometry based on staining for CD10, CD20, CD21 and CD27 was used for B cell profiling (transitional T1; transitional T2/T3; naïve; classical memory; activated memory; atypical memory; plasmablasts). Vaccine responses were tested using fluorescent tetanus toxoid C fragment (TTCF) oligomers.

Results: HEU born to mothers with peak VL ≥40 copies/ml in pregnancy (n=11) had higher or tended toward higher frequencies of classical (p=0.0081) and activated memory B cells (p=0.0596), and plasmablasts (p=0.0454) in CB as compared to the <40 group (n=13). However, the latter had a significantly higher frequency of total B cells (p=0.0410) in CB. At 6 months of age (n=9), HEU born to mothers with peak VL ≥40 copies/ml had or tended toward higher frequencies of naive B cells (p=0.0371) and TTCF-specific naïve B cells (p=0.0564). TTCF oligomers revealed the presence of tetanus-specific B cells in all HEU children.

Discussion: The degree of exposure to maternal HIV in utero was associated with differential frequencies of various B cell subsets in HEU that waned over time, suggesting that HIV antigens have a transitory effect on B cell differentiation and/or homeostasis. TTCF-specific responses are compatible with immune competence and vaccine efficacy.

BS2.6

Reconstitution of gut IL-22/IL-22R axis with early initiation of antiretroviral therapy, but evidence of epithelial damage and inflammation

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IL-22 is a tissue cytokine that maintains the epithelial barrier and promotes tissue regeneration. It binds to IL-22 receptors (IL-22R) expressed on epithelial cells, but can also bind to regulatory IL-22 binding protein (IL-22BP). Soon after HIV infection, IL-22 producing Th22 and other immune cells in the gut are drastically depleted, and their loss may promote microbial translocation, immune activation and HIV disease progression. We hypothesized that gut Th22 cells and IL-22 signaling was disrupted to impair the gut epithelial regneration and contribute to inflammation in HIV positive individuals on effective ART.

ART-naïve men with early HIV infection were randomized in a double-blind manner to receive standard ART with either raltegravir and maraviroc, or placebo, for 48 weeks [NCT01154673]. In a predefined substudy, paired blood and sigmoid biopsies were collected from participants at baseline and week 48 (n=21), and from HIV-uninfected controls (n=10). Mucosal CD4 T cell immunology (Th1, Th17 and Th22 cells), blood markers of inflammation (IL-6, D-dimer), gut epithelial integrity (I-FABP) and tissue levels of IL-22R and IL-22BP were measured. Intensified ART did not alter gut or systemic endpoints so participants in two study arms were pooled for data analysis.

All participants had undetectable viral load and increased CD4 count after ART. Gut Th22 and IL-22 producing cells were depleted at baseline but were normalized after 1 year of effective ART, however blood markers of gut epithelial integrity (I-FABP) and inflammation (IL-6) remained elevated. Contrary to our hypothesis, IL-22R and IL-22BP in the gut tissue were similar before and after ART to uninfected controls.

Gut Th22 cells are restored after 1 year of ART initiated during early HIV infection, and IL-22 signaling to epithelial cells is not disrupted. Other pathological mechanisms outside of the gut IL-22 axis may contribute to epithelial barrier damage and inflammation during ART.

BS2.7

Evolution-Guided Structural And Functional Analyses Of The HERC Restriction Factor Family Identifies Specificity Determinants Of Anti-HIV-1 Activity

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Human HERC5 is a host restriction factor that inhibits the replication of human immunodeficiency virus type 1 (HIV-1) by two independent mechanisms. The first mechanism inhibits nuclear export of incompletely-spliced HIV-1 RNA, whereas the second mechanism inhibits an early stage in virus assembly by modifying its structural protein Gag with the ubiquitin-like molecule ISG15. To gain a better understanding of the evolution and function of HERC5, we performed phylogenetic, structural and functional analyses of the entire small HERC family, which includes HERC3, HERC4, HERC5 and HERC6. We demonstrated that HERC3 and HERC4 have an ancient marine origin of >476 million years ago, whereas HERC5 emerged ~413 million years ago in coelacanth and HERC6 ~430 million years ago in ray-finned fish. Evolution-guided structural and functional analyses showed that HERC3, HERC4 and HERC5, but not HERC6, inhibited HIV-1 replication. Structure-guided mutagenesis and functional analyses identified key amino acid determinants of antiviral activity. Together, our data shows that the *HERC* family has one of the oldest known marine origins for an antiviral gene family in vertebrates and has undergone gene duplication, deletion and innovation events throughout its evolution.

BS2.8

The ABL Kinase Inhibitor Dasatinib Inhibits HIV-1 infection in Humanized NSG Mice

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Background: Previously we have shown that dasatinib, an inhibitor of the Abelson family (ABL) kinases approved for treatment of chronic myelogenous leukemia, reduces HIV-1 infection *in vitro*. However the role of c-ABL, or the related kinase ARG, remains unknown during infection of primary $CD4^+$ T-cells. Moreover it has never been tested whether dasatinib inhibits HIV-1 *in vivo*.

Methods: $CD4^+$ T-cells isolated from PBMCs of healthy donors were electroporated with siRNA targeting c-ABL or ARG, then activated with anti-CD3/anti-CD28/IL-2. After 48hrs, cells were infected with JR-FL (R5) carrying a luciferase reporter. 24hrs post-infection, we quantified reverse transcripts, 2-LTR circular DNA and integrated virus by qPCR. Luciferase readings were measured 72hrs post-infection. In other experiments, we isolated PBMCs from treatment naïve, HIV-1 infected patients, activated the cells, and administered dasatinib twice a week. Cell viability and p24 production were measured over three weeks. Lastly, NSG mice engrafted with human hematopoietic stem cells ($hCD34^+$) were infected with Ba-L (R5) and injected with dasatinib (25mg/mouse/daily) starting 4-5 weeks post-infection. Plasma viral load was quantified by qRT-PCR.

Results: 24hrs post-infection, siRNA knockdown of c-ABL or ARG had no effect on JR-FL reverse transcripts in $CD4^+$ T-cells. However 2-LTR circles increased 4-fold and integrated virus decreased 9-fold. This coincided with 60% reduced luciferase activity. Chronically infected PBMCs given dasatinib showed significantly reduced p24 levels over 21 days, and undetectable p24 with 100nM dasatinib. Cell viability was unaffected. Within a week of daily dasatinib injections, Ba-L infected NSG mice showed as much as a 90% reduction in viral load relative to control.

Conclusions: We provide *in vitro*, *ex vivo* and *in vivo* evidence that c-ABL and ARG are very appealing targets to reduce HIV-1 infection. Further research should explore how kinase inhibitors targeting the ABL family could be included in combination therapies when HIV-1 drug resistance develops.

Clinical Sciences: Co-infection

Sciences cliniques : Coinfection

CS2.1

Asymptomatic Neurosyphilis is Common in HIV/Syphilis Co-infection: A Feasibility and Pilot Cohort Study

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Background: HIV/syphilis co-infection can be complicated by asymptomatic neurosyphilis (ANS), but there is inadequate evidence to determine which neurologically asymptomatic patients should undergo diagnostic lumbar puncture (LP). To plan for a larger prospective cohort study addressing this question, we conducted a pilot study to determine the feasibility of LPs in this population and to estimate the prevalence of ANS among neurologically asymptomatic co-infected adults.

Methods: Neurologically asymptomatic HIV-infected adults newly diagnosed with syphilis were recruited at two

sites in Toronto and Edmonton between November 1, 2011 and November 1, 2014. Consenting participants underwent diagnostic LP as soon as possible after diagnosis, and completed an acceptability questionnaire and a telephone interview to assess for post-procedure headache. $75 compensation was provided for the procedure. ANS was defined as reactive VDRL, reactive FTA-Abs or leukocyte count >10/uL in cerebrospinal fluid (CSF).

Results: 24 eligible patients agreed to participate in the study, of whom all were men who have sex with men. Median (IQR) age was 36 (30,47) years, CD4 count was 424 (166,823) cells/μL, and RPR titre was 1:64 (1:4,1:256). Stage of syphilis was primary, secondary, and early latent in 2/24 (8.3%), 9/24 (37.5%) and 6/24 (25.0%), respectively, with 1/24 late latent (4.2%), 2/24 latent of unknown duration (8.3%) and three missing. Among 19 participants who consented to LP, 11 had received treatment within 8 days prior to LP (9 benzathine penicillin, 2 doxycycline) and 9/19 (47.4%) reported post-LP headache. ANS was diagnosed in 6/19 patients (31.6%), based on reactive CSF VDRL and FTA-Abs (n=5) or WBC (n=1).

Conclusions: ANS may be common in HIV/syphilis co-infected adults and LPs are feasible in this population. Research to develop a clinical prediction rule is needed to determine which co-infected patients require an LP in the absence of neurological symptoms.

CS2.2

Rates and Risk Factors for Hepatitis C Re-Infection or Late Relapse after Sustained Virologic Response to Treatment among HIV Co-Infected Canadians

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Background: New treatments for hepatitis C virus (HCV) infection are effective but benefits may be mitigated by re-infection. We describe rates and predictors of re-infection after sustained virologic response (SVR) in a co-infected cohort.

Methods: We included subjects from the Canadian Co-Infection Cohort who were enrolled from 2003-2014 and had a confirmed SVR and ≥ 1 follow-up HCV RNA measurement. Subjects were followed from SVR to re-infection, defined as a single detectable HCV RNA measurement. Demographic, substance abuse, and behavioral risk factors for re-infection were self-reported semi-annually. HCV RNA testing was performed every 6 months post-SVR. Cox models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for re-infection.

Results: 157 subjects with SVR were followed for 383 person-years (PYs; interquartile range [IQR]: 1.0-3.3 years). The median age was 46 years (IQR: 39-51) and 84% were male. The median time from estimated HCV infection to SVR was 17 years (IQR: 9-27). We identified 20 re-infections for an incidence rate of 5.2 per 100 PYs (95% CI: 3.4–8.1). 29% reported injection drug use (IDU), 13% shared needles or other drug equipment and 51% reported unprotected sex post-SVR. Substance abuse and sharing equipment after SVR increased the risk of HCV re-infection substantially (Table). Among MSM, IDU appeared to be the principal risk factor for re-infection although inference was limited.

Conclusion: IDU is an important driver of HCV re-acquisition. To realize the potential of new therapies to cure, HCV treatment will need to be paired with broader harm reduction programs.

Hazard Ratios and 95% Confidence Intervals for HCV Re-Infection Risk Factors after Sustained Virologic Response in Canadian Co-Infection Cohort (n=157)

	Unadjusted		Adjusted		MSM-Restricted Adjusted	
	HR	95% CI	HR	95% CI	HR	95% CI
Age (per 5 years)	1.04	0.81, 1.35				
Male Sex	1.54	0.45, 5.32				
Antiretroviral Therapy Use	0.25	0.09, 0.70	0.37	0.13, 1.06	0.73	0.14, 3.90
Detectable HIV Viral Load	1.35	0.45, 4.07				
Injection Drug Use	4.79	1.90, 12.1	3.36	1.22, 9.21	4.64	0.92, 23.2
Sharing Injection Equipment	8.11	1.78, 37.0				
Snorting/Sniffing Illicit Drugs	3.03	1.13, 8.09	1.89	0.66, 5.43	0.94	0.17, 5.29
Sharing Snorting Equipment	5.38	1.53, 18.9				
Recent STI diagnosis	3.21	0.70, 14.7			1.74	0.19, 15.6
Unprotected sex	0.94	0.30, 2.92				

CS2.3

A Comparison of the Performance of an HPV E6/E7 mRNA Assay With a DNA-based Assay on Anal Samples in HIV-Positive Men Who Have Sex With Men (MSM)

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Background: Persistent infection with high-risk HPV (HR-HPV) is responsible for most anal cancers, which disproportionately affect HIV-positive men who have sex with men (MSM). Given the high prevalence of anal HR-HPV infection in MSM, and the suboptimal performance of cytology in predicting dysplasia, there is a need for improved diagnostics. HPV E6/E7 mRNA testing is felt to represent a more specific test for persistent HPV, but there is no published data on the use of the specific assay examined herein in the anal canal. The aim of this study was to compare the performance of an HPV mRNA assay to a DNA-based assay on archived samples from HIV-positive MSM.

Methods: Archived anal cytology samples were collected from HIV-positive MSM attending a large anal cancer screening clinic between 2011-2014. These samples were stored in PreservCyt solution at room temperature, and were tested in parallel with the mRNA-based Aptima® HPV Assay and the cobas® HPV DNA-based assay in late 2014.

Results: Samples from 216 participants were analyzed: 155 (71.7%) were positive via mRNA testing, and 172 (79.6%) were positive via DNA testing. For detection of cytologic high-grade squamous intraepithelial lesion (HSIL), the sensitivity, specificity, positive predictive value, and negative predictive value was 78.7%, 32.0%, 45.2%, and 67.8%, respectively, for the mRNA assay, and 82.8%, 18.7%, 41.9%, and 60.5%, for the DNA assay. The sensitivities of both assays for detecting histologic high-grade dyplasia were similar (92.0% vs. 91.8%), but specificity was higher for the mRNA assay (38.0% vs. 23.5%; $p < 0.05$)

Conclusions: HPV E6/E7 mRNA was as sensitive, and more specific, than DNA testing for detecting high-grade dysplasia. Given the reliance on HPV testing as an adjunct to cytology in anal cancer screening, this novel assay may represent an improved method by which HIV-positive MSM undergoing screening can be risk-stratified to further management.

CS2.4

Timing of Hepatitis B and C Diagnosis Relative to Hepatocellular Carcinoma Diagnosis in the BC Hepatitis Testers Cohort (BC-HTC)

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Background: Early diagnosis of hepatitis B (HBV) and hepatitis C (HCV) followed by treatment prevents late stage liver disease. We measured the timing of HBV and HCV diagnoses relative to detection of hepatocellular carcinoma (HCC) as an indicator of late hepatitis diagnosis.

Methods: The British Columbia Hepatitis Testers Cohort (BC-HTC) consists of 1,417,780 individuals tested for HCV, HIV and/or reported as a case of HBV, HCV, HIV or tuberculosis from 1990 and linked with medical visits, hospitalizations, cancers, prescription drugs and mortality. Late hepatitis diagnosis was defined as HBV or HCV diagnosis ≥2 years prior to or after HCC diagnosis. HCV diagnosis date was the date of the first positive test. HBV diagnosis date was the date HBV was reported to public health.

Results: Between 1992 and 2011, 2,250 cases of HCC were diagnosed; 612 (27%) were HBV positive, 868 (39%) HCV positive, and 47 (2%) had both. Overall, 659/34,775 HBV cases (1.9%) and 915/65,842 HCV cases (1.4%) developed HCC. Among HBV and HCV cases with HCC, 45% and 31% respectively were late diagnoses. HBV late diagnosis declined from 100% in 1992 to 53% in 2000 to 24% in 2011. HCV late diagnosis declined from 100% in 1992 to 30% in 2000 to 13% in 2011. In the multivariable logistic regression, late hepatitis diagnosis was associated with HBV mono-infection and HBV/HCV co-infection vs. HCV mono infection while birth years <1945 and 1945-1964 vs. ≥1965; those with illicit drug use, and HIV co-infection were less likely to be diagnosed late.

Conclusion: People with risk activities were diagnosed earlier highlighting the impact of risk based screening; late diagnoses also decreased over time. However, the high percentage of late diagnoses for HBV and HCV indicates a significant pool of undiagnosed infections where secondary prevention and treatment could improve outcomes.

CS2.5

Ledipasvir/Sofosbuvir with Ribavirin for 12 Weeks Is Effective and Safe in Treatment-Naïve Genotype-3 HCV-Infected Patients in Canada

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Background and Aims: Interferon-free regimens have demonstrated lower response rates in genotype (GT) 3 HCV-infected patients as compared to GT1 patients. Ledipasvir/sofosbuvir (LDV/SOF) with ribavirin (RBV) for 12 weeks resulted in a 100% SVR12 rate among treatment-naïve GT3 patients with and without cirrhosis in a single center Phase 2 trial. In this study, we evaluated the safety,

tolerability and efficacy of LDV/SOF+ RBV for 12 weeks in GT 3 patients at 15 sites in Canada.

Methods: Treatment-naïve GT3 HCV-infected patients with or without compensated cirrhosis received open-label LDV/SOF+RBV for 12 weeks. The primary endpoint was SVR12. Secondary endpoints included safety, tolerability, viral resistance, and additional efficacy outcomes.

Results: 111 patients were randomized and treated: 61% male, 70% white, 23% Asian, 62% carried the non-CC IL28B allele, and 34% had compensated cirrhosis. Overall, the SVR4 rate was 92% (102/111). SVR4 rate was 97% (71/73) for non-cirrhotics, 82% (31/38) for cirrhotics. Virologic outcomes are shown in the Table 1. One patient (<1%) discontinued treatment due to liver cancer (hepatocellular carcinoma or cholangiocarcinoma) and died 22 days post-treatment. Adverse events (AEs) occurring in >10% of patients were fatigue, headache, nausea, insomnia, dizziness, diarrhea and irritability. Four patients had serious AEs, none was related to treatment. Fourteen (14%) patients experienced grade 3 or 4 laboratory abnormalities, the majority of which were consistent with RBV therapy.

Conclusions: LDV/SOF+ RBV for 12 weeks in treatment-naïve patients with chronic HCV GT 3 infection led to high SVR4 rates. Treatment was safe and well-tolerated; the profile was consistent with that observed in the LDV/SOF+RBV groups in the Phase 3 studies. Complete SVR12 data will be presented.

CS2.6

Tobacco Smoking is Not Associated with Accelerated Liver Disease in HIV-Hepatitis C Co-Infection: A Longitudinal Cohort Analysis

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Background: Tobacco smoking has been shown to be an independent risk factor for liver fibrosis in Hepatitis C (HCV) infection in some cross-sectional studies. No longitudinal study has confirmed this relationship and the effect of tobacco exposure on liver fibrosis in HIV-HCV co-infected individuals is unknown.

Methods: The study population consisted of participants from the Canadian Co-infection Cohort study (CTN 222), a multicenter longitudinal study of HIV-HCV co-infected individuals from 2003-2014. Data were analyzed for all participants who did not have significant fibrosis or end-stage liver disease (ESLD) at baseline. The association between time-updated tobacco exposure (ever vs. non-smokers and pack-years) and progression to significant liver fibrosis (defined as an aspartate-to-platelet ratio index (APRI) ≥1.5) or ESLD was assessed by pooled logistic regression.

Results: Of 1072 participants included, 978 (91%) had ever smoked, 817 (76%) were current smokers and 161 (15%) were previous smokers. Tobacco exposure was not associated with accelerated progression to significant liver fibrosis (APRI ≥ 1.5) nor with ESLD when comparing ever vs. never smokers or increases in pack-years smoked (Table 1). Both time-updated alcohol use in the previous 6 months and presence of detectable HCV RNA were associated with APRI score ≥ 1.5 (OR [95% CI]: 1.56 [1.04, 2.07] and 3.54 [1.64, 5.41], respectively). Tobacco smoking was not associated with accelerated liver disease even stratified by alcohol use (Table 1).

Conclusions: Tobacco exposure does not appear to be associated with accelerated progression of liver disease in this prospective study of HIV-HCV co-infected individuals.

Table 1: Association between tobacco smoking and progression to significant liver fibrosis (APRI ≥ 1.5) or end-stage liver disease (ESLD)*

Outcome		APRI ≥ 1.5		ESLD
Sample	All	No alcohol use	Alcohol use	All
Ever vs. never smoked	1.06 (0.43, 1.69)	0.77 (0.06, 1.48)	1.23 (0.26, 2.20)	1.20 (0.21, 2.18)
Pack-years** (per 10 pack-years)	1.05 (0.97, 1.14)	1.04 (0.91, 1.18)	1.07 (0.94, 1.19)	0.94 (0.83, 1.05)

*adjusted for baseline characteristics (sex, age, HCV duration and income) and updated variables (alcohol use, intravenous drug use, CD4 count, HIV viral load, detectable HCV RNA, and glucose intolerance)

**Centred at mean=25.8 pack-years if ever smoker, 0 if never smoker

CS2.7

Real setting experience of Hepatitis C treatment with Interferon-Free DAA in HCV mono and HIV-HCV-coinfected patients

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Background: Few studies have examined the impact of new interferon-free direct-acting antiviral (DAA) treatments in clinical practice. The aim of this study is to evaluate the efficacy of DAA regimens in real life settings in HCV-mono and HIV-HCV-coinfected individuals.

Methods: We prospectively assessed all HCV-infected patients attending our clinic receiving INF-free DAA treatments. Patients enrolled in RCTs were excluded. Primary outcome was sustained virologic response (SVR@12w) by intent-to-treat analysis. Comparisons among mono and co-infected patients were assessed by chi-square.

Results: 249 DAA treatments were included. Patients were mainly male (70%) with mean age of 53 years (IQR 48-59). The majority of patients were infected with HCV genotype 1 (74%) and were treatment naïve (64%). 99 (40%) patients were cirrhotic, 61 (25%) were HIV-HCV-coinfected and 39 (20%) were active injection drug users. Patients received: SOF/LDV (32%), SIM+SOF (26%), SOF+RBV (26%), SOF/LDV+RBV (8%) or OBV/PTV/r+DSV±RBV (8%). At 12w post-treatment follow-up, data was available for 156 patients. Overall, 133/156 patients (85%) achieved SVR, 8 (5%) relapsed and 6 (4%) failed to respond to treatment. Nine patients (6%) were lost to follow-up and were considered treatment failures. The SVR rates for each regimen were: SOF/LDV (32/38, 84%), SIM+SOF (55/65, 85%), SOF+RBV (34/40, 85%), SOF/LDV+RBV (8/8, 100%), OBV/PTV/r+DSV±RBV (4/5, 80%). No difference was observed in the SVR rate among treatment regimens (p=0.82), nor according to treatment history, injection drug use nor genotype. Cirrhotic patients had lower SVR (78% vs. 91% for non-cirrhotic, p=0.02), moreover, coinfected patients with cirrhosis had significantly lower SVR rates (85% for HCV-monoinfected vs. 64% for HIV-HCV-coinfected, p=0.04). However, in the absence of cirrhosis, there was no effect of HIV-HCV-coinfection on SVR (91% for HCV-monoinfected vs. 90% for HIV-HCV-coinfected, p=0.75).

Conclusions: DAAs offer high SVR in clinical settings, though lower than in RCTs. HIV-coinfection doesn't preclude the SVR, except for cirrhotic patients.

CS2.8

Association of Fibroblast Growth Factor 23 and Serum Ferritin with Liver Fibrosis diagnosed by Transient Elastography in HIV/HCV Co–Infected Patients

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Background: HIV/HCV co-infection is characterized by a faster progression of liver fibrosis towards cirrhosis. Identification of biomarkers associated with liver fibrosis is pivotal for prognosis and management.

Methods: We studied correlation of iron and inflammatory serum biomarkers (hepcidin, iron, ferritin, transferrin saturation, fibroblast growth factor 23 (FGF23), interleukin-6 and tumor necrosis factor-α) with significant liver fibrosis diagnosed by transient elastography (TE). We selected these biomarkers because iron and inflammatory status are known to affect liver damage. We included HIV/HCV co-infected patients who were HCV RNA positive, on antiretrovirals and had HIV viral load <50 cp/mL. Pairwise correlation and linear regression were used to explore association with liver fibrosis.

Results: 45 consecutive patients (mean age 47 years, 78% male) were included. Median TE measurement was 7 kPa (interquartile range 5.2-14). 48% of the patients had significant liver fibrosis. Liver fibrosis was significantly correlated with ferritin (r=0.51, p=0.001), transferrin saturation (r=0.36, p=0.003), FGF23 (r=0.36, p=0.02) and interleukin-6 (r=0.42, p=0.007). The results of multivariate analysis and relative regression coefficients are shown in the Table. After adjustments, ferritin and FGF23 were independently associated with liver fibrosis.

Conclusion: Serum ferritin and FGF23 are positive independent predictors of liver fibrosis in HIV/HCV co-infected patients. These data are consistent with recent findings identifying serum ferritin as independent predictor of advanced fibrosis and mortality in chronic liver diseases of other etiologies. They also suggest that serum FGF23 has a potential as biomarker for liver fibrosis in HIV/HCV co-infected patients. Larger scale studies are required to validate our data.

	Adjusted regression coefficient	95% CI	p
Serum Ferritin	0.04	0.02-0.06	<0.001
FGF23	0.011	0.002-0.021	0.02
Hepcidin	-0.25	-0.53-0.0034	0.08
Interleukin 6	0.34	-0.124-0.810	0.14

Epidemiology and Public Health: Social and Structural Correlates of HIV Risk and Care

Épidémiologie et santé publique : Corrélats sociaux et structurels du risque et des soins touchant le VIH

EPH2.1

The effect of engagement in an HIV/AIDS integrated health program on plasma HIV-1 RNA suppression among HIV-positive people who use illicit drugs

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Background: HIV treatment-as-prevention efforts emphasize prompt diagnosis of infection and immediate access to antiretroviral therapy (ART) for HIV-positive individuals in order to curb the likelihood of morbidity, mortality and onward viral transmission through suppression of HIV RNA plasma viral loads (VL). However, the possible role of harm reduction-based programs in this objective among people

living with HIV/AIDS who use illicit drugs has not yet been well evaluated.

Objective: To estimate the effect of being a client of the Dr. Peter Centre (DPC; an HIV/AIDS-focused adult integrated health program) on VL suppression among antiretroviral therapy (ART)-exposed HIV-positive people who use illicit drugs (PWUD) in Vancouver, Canada.

Methods: Data were derived from the ACCESS study, a community-recruited prospective cohort of HIV-positive PWUD. A marginal structural model using inverse probability of treatment weights was used to estimate the longitudinal relationship between being a DPC client and exhibiting an HIV-1 RNA viral load < 50 copies/mL plasma.

Results: Between 2005 and 2014, 746 HAART-exposed participants were included in the study, among whom 269 (36.1%) reported being a DPC client at some time during the study period. After adjusting for various socio-demographic, behavioural and clinical variables, a marginal structural model estimated a 1.60 greater odds of achieving VL suppression (95% confidence interval: 1.24 – 2.06) among DPC clients.

Conclusions: We found that HIV-positive PWUD who attended the DPC were more likely to achieve VL suppression compared to those who did not. Our findings demonstrate that participating in an innovative HIV/AIDS-focused adult integrated health program that provides a broad range of clinical, harm reduction, and support services may contribute to optimizing the benefits of ART on HIV/AIDS-associated morbidity, mortality and viral transmission among PWUD.

EPH2.2

A population-based study evaluating the impact of physician specialty and physician HIV experience on the delivery of care for people living with HIV in Ontario

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Context: Physician specialty and physician HIV experience are often positively associated with HIV-specific outcomes but negatively associated with primary care outcomes. Our objective was to explore the association between physician specialty and family physician HIV experience and the quality of care to people with HIV.

Methods: A validated case ascertainment algorithm was applied to provincial administrative data to identify people with HIV from 1 April 2009 to 31 March 2012 (n=13,480). We linked patients to family physicians and assigned them to one of five possible care models. We used multivariable hierarchical logistic regression analyses to evaluate the following outcomes: receipt of any antiretroviral (ART), adherence to cancer screening, and health services utilization. We used interaction models to evaluate the modification of this association by level of family physician HIV experience (<=5, 6-49, 50+ patients)

Results: The odds of colorectal cancer screening was higher for patients in models with predominantly family physician care than for those with exclusively specialist care (adjusted OR (AOR)=3.12, 95% CI (1.90 to 5.13)). The odds of having one emergency department visit did not differ among models, although the odds of hospitalization were lower among patients who saw exclusively family physicians (AOR=0.23, 95% CI (0.14 to 0.35). The odds of receiving ART was lower among patients in models with predominantly family physician care (AOR=0.15, 95% CI (0.12 to 0.21), and receipt of ART was significantly lower among those receiving care from family physicians with <=5 patients (mean 34%, 95% CI (30 to 39%)) and 6-49 patients (40%, 95% CI 34 to 45%) compared to those with 50+ patients (77%, 95% CI 74-80%). Other outcomes were unrelated to family physician HIV experience.

Conclusions: How care is delivered influenced quality of care**;** future work must determine the best models for integrating and delivering comprehensive care for people with HIV.

EPH2.3

The Impact of Drug Coverage on Viral Suppression: Findings from the Ontario HIV Treatment Network Cohort Study (OCS)

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Background: For the benefits of antiretroviral therapy (ART) to be realized, uninterrupted access is critical. In Ontario, given that there is no universal coverage of prescription drugs including ART, we investigated the effect of drug coverage on viral suppression (sVL).

Methods: The OCS is a multi-site HIV clinical cohort. Patients in Ontario without employment coverage may be eligible for coverage through the government sponsored Ontario Drug Benefit (ODB, 100% coverage) or Trillium (deductible based on household income) programs. Remaining individuals pay out of pocket. Among participants interviewed in 2008-12, had known or imputable (LOCF) drug coverage and who were on ART, we estimated the annual prevalence with sVL (<200 copies/mL) as of the last VL each year. We calculated prevalence ratios according

to time-updated socioeconomic and behavioral factors, adjusted for clinical characteristics, using multivariable generalized estimating equations with a log-link function.

Results: A total of 1,281 participants were included with 3,258 person-years. Univariately, compared to coverage via an employer, individuals covered through ODB (Prevalence Ratio (PR), 95% Confidence Interval (CI): 0.95, 0.92-0.97) or who paid solely out of pocket (0.92, 0.85-0.98) were less likely to be suppressed. After multivariable adjustment, paying out of pocket remained independently associated (Adjusted Prevalence Ratio (APR), 95% CI: 0.92, 0.86-0.98). Other prognostic factors independently associated with sVL are shown below.

Conclusions: Given the pivotal place of ART in optimizing HIV treatment outcomes and the broader population health implications, our findings indicate that universal coverage for ART is critical and requires urgent exploration in our setting.

Table 1: Factors associated with suppressed viral load

		Prevalence Suppressed	Unadjusted Prevalence Ratio (95% CI)	Adjusted* Prevalence Ratio (95% CI)
Drug Coverage	Employer	96.2%	1	1
Co-payment	94.2%	0.97 (0.93-1.01)	0.96 (0.91-1.01)	
Ontario Drug Benefit	91.8%	0.95 (0.92-0.97)	0.97 (0.94-1.00)	
Out of Pocket	90.4%	0.92 (0.85-0.98)	0.92 (0.86-0.98)	
Trillium	95.7%	0.99 (0.97-1.02)	1.00 (0.97-1.03)	
Age at Follow-up	<35	87.2%	1	1
35-49	93.1%	1.06 (1.01-1.11)	1.06 (1.01-1.11)	
≥50	96.2%	1.10 (1.04-1.15)	1.08 (1.02-1.14)	
Sex/Orientation	MSM	95.3%	1	1
Female	91.2%	0.95 (0.91-0.98)	0.96 (0.93-0.99)	
Male: non MSM/ Unknown	91.4%	0.94 (0.91-0.98)	0.94 (0.93-0.99)	
Mental Health Concerns	No	95.0%	1	1
Yes	90.5%	0.95 (0.92-0.97)	0.96 (0.94-0.98)	
Cigarette Smoking	Current smoker	90.7%	0.95 (0.92-0.97)	0.95 (0.92-0.98)
Occasional smoker	91.2%	0.95 (0.90-1.01)	0.98 (0.93-1.04)	
Former smoker	97.8%	1.03 (1.01-1.05)	1.02 (1.01-1.04)	
Never smoked	95.1%	1	1	
Drug Use	No drug use	94.4%	1	1
Yes, non IDU	93.7%	0.99 (0.96-1.03)	1.01 (0.97-1.05)	
Yes, IDU	80.4%	0.86 (0.78-0.94)	0.91 (0.84-0.99)	

*Adjusted for all covariates shown and ethnicity, immigration status, employment status, living alone, alcohol use, years on ART, and clinical site; MSM=Men who have Sex with Men; IDU= Injection Drug Use

EPH2.4

Multilevel correlates of delayed access to HIV-related care among women living with HIV in the Greater Toronto Area, Canada

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Background: Timely entry into HIV-related healthcare is necessary to optimize the health and well-being of women with HIV. Individual, social, and structural barriers may influence access to HIV-related healthcare within urban contexts of high service availability. This study seeks to identify multilevel correlates of delayed access to HIV-related care among women with HIV from the Greater Toronto Area (GTA), Ontario, Canada.

Methods: We analysed baseline survey data of GTA women from the Canadian HIV Women's Sexual and Reproductive Health Study (CHIWOS), a community-based participatory longitudinal cohort study (n=294/1425). The outcome variable examined in this study was delayed access to HIV-related care, defined as >3 months between time of diagnosis and time of first access. We conducted bivariate analyses using chi-square and ANOVA to explore the association between sociodemographic, individual, social, structural, and health factors and delayed access to HIV-related care. A multivariate logistic regression model was then built by entering all time-invariant variables with a bivariate p-value <0.20.

Results: One-quarter (n=75, 25.5%) of women in the GTA reported delayed access to HIV-related care. Women with delayed access to care had higher depression (CES-D) [F(1,284)=5.71, p<.05)] and lower resili-

ency (RS-10) [F(1,290)=8.42, p<.01], social support (MOS-SSS) [F(1,284)=13.14, p<.001], physical health (SF-12) [F(1,288)=3.94, p<.05], and mental health (SF-12) [F(1,288)=15.68, p<.001] scores, compared to women with timely access to care. In multivariate analyses, women diagnosed ≥6 years ago had higher odds of delayed access to care [OR:5.3,95%CI:2.5-11.2] compared to those diagnosed <6 years ago and women of non-white ethnicity (Black, Aboriginal, and other ethnicities) had higher odds of delayed access to care [OR:2.1,95%CI:1.1-4.0] compared to Caucasian women.

Implications: Our findings document multilevel factors associated with delayed access to care for women with HIV in the GTA. Understanding these factors can inform interventions to improve timely access to HIV-related care and optimize early diagnosis.

EPH2.5

The Cedar Project: Longitudinal health outcomes associated with childhood neglect among young Indigenous people who use drugs in BC

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Background: Indigenous leaders are concerned that historical and lifetime traumas contribute to the HIV/HCV epidemics among their young people. To our knowledge, no previous studies have addressed the longitudinal effects of emotional neglect (EN) and physical neglect (PN) on HIV risk among young Indigenous people who use drugs.

Methods: The Cedar Project is a cohort of young Indigenous people (aged 14-30) who use drugs in Vancouver, Prince George, and Chase, BC. We used the Childhood Trauma Questionnaire (CTQ) to determine experiences and severity levels (none; low/moderate; severe) of childhood EN and PN. Generalized linear mixed effects models explored associations between severity of EN and PN with HIV risk between 2003-2012, adjusting for confounders.

Results: Overall, 266 participants (53% women; mean age 23 years) completed the CTQ and at least one follow-up. For EN, 28.4% reported none, 51.1% reported low/moderate, and 17.8% reported severe experiences. For PN, 20.8% reported none, 36% reported low/moderate, and 39.4% reported severe experiences. Severe PN was associated with having a parent who had attended residential school (p=0.002). In multivariate analyses, an increase of one level of EN severity was associated with being involved in sex work (AOR: 1.88; 95% CI: 1.041-3.412), and injection drug use (AOR: 2.0; 95% CI: 1.113-3.849). A one level increase of PN severity was associated with homelessness (AOR: 1.33; 95% CI: 1.014-1.740); binge drinking (AOR: 1.5; 95% CI: 1.094-2.098); blacking out while drinking (AOR: 1.5; 95% CI: 1.082-2.105); inconsistently using condoms (AOR: 1.52; 95% CI: 1.025-2.258), and; binge injection (AOR: 1.64; 95% CI: 1.164-2.325).

Conclusion: Childhood neglect continues to negatively impact the health of young Indigenous people and contributes significantly to their vulnerability to HIV and HCV infection. The urgent need to develop public health responses that incorporate both historical trauma and cultural strengths to reduce risks cannot be overstated.

EPH2.6

Condomless sex among virally suppressed women living with HIV with serodiscordant sexual partners

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Background: Sexual HIV transmission risk approaches zero with achievement of combination antiretroviral therapy (cART)-related viral suppression. Awareness of cART prevention benefits and its influence on condom use among women living with HIV (WLWH) remain unexplored in Canada. We estimated the prevalence and correlates of condomless sex with sero-discordant partners among WLWH reporting cART-related viral suppression.

Methods: We used baseline survey data from the community-based Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS) of WLWH in BC, Ontario, and Quebec. We included women self-reporting vaginal/anal sex with ≥1 HIV-negative/unknown status partner in the prior 6 months, and self-reporting cART-related viral suppression. We excluded participants exclusively reporting female sexual partners, or missing condom-use data. Condomless sex was defined as self-reporting <100% condom use in the prior 6 months. The primary explanatory variable was awareness of prevention benefits of cART ("believe that cART makes HIV transmission risk a lot lower"). Logistic regression identified factors independently associated with condomless sex.

Results: We included 271 (34%-BC, 35%-Ontario, 31%-Quebec) of 1425 CHIWOS participants (notably excluding 843 reporting no recent vaginal/anal sex, 182 without serodiscordant partners, and 100 without cART-related suppression). Median age was 41 (IQR:34-47), 51% were in a relationship, and 26% expressed pregnancy intentions. Overall, 77% were aware of the prevention benefits of cART and 55% self-reported condomless sex. Of women aware of cART prevention benefits, 63% reported

condomless sex, compared to 32% of women not aware (p<0.001). Factors independently associated with condomless sex included awareness of cART prevention benefits, BC residence, Caucasian ethnicity, ≥high-school education, and being in a relationship.

Conclusions: Among virally-suppressed WLWH, awareness of cART prevention benefits is associated with condomless sex. While this awareness offers women another safer-sex option to minimize HIV transmission risk to serodiscordant partners, this option is not utilized consistently across the diversity of Canadian WLWH.

EPH2.7

Coercive sex as a mode of HIV acquisition among a cohort of women with HIV in Canada: an under-recognized public health concern

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Background: Worldwide women experience high rates of violence related to entrenched gender inequities. This violence includes coercive sex, which may lead to HIV acquisition. We assessed the prevalence of and factors associated with HIV acquisition via coercive sex among women with HIV enrolled in a Canadian cohort.

Methods: Baseline survey data were analyzed for women with HIV (≥16 years) with data on mode of HIV acquisition, enrolled in a community-based research cohort study (CHIWOS) in British Columbia (BC), Ontario (ON), and Québec (QC). Coercive sex was assessed through self-report of 'non-consensual sex' as a mode of HIV acquisition or violence as a child or adult resulting in HIV. Multivariable logistic regression was used to identify factors associated with self-reported coercive vs. consensual sex as the mode of HIV acquisition.

Results: Of 1425 participants, 1,330 were analyzed (26 -BC, 49%-ON, 25%-QC) (median age was 42 (IQR=35-50) years; 23.5% were Indigenous 26.3% African/Caribbean/Black and 43% White). Coercive sex was the third dominant mode of HIV transmission at 16.5% (N=219) (vs. 51.6%-consensual sex, 19.7%-sharing needles, 5.3%-blood transfusion, 3.8%-perinatal, 1.3%-contaminated needles, 1.6%-don't-know/PNTA, 0.4%-other). In multivariable analysis, covariates significantly associated with acquiring HIV from coercive vs. consensual sex were: being from BC vs. ON [aOR=2.5 95% CI=1.5-4.0]; being of African/Caribbean/Black ethnicity vs. White [aOR=3.3 95% CI=1.5-7.2], living in Canada<5 years vs. being Canadian born [aOR=3.7; 95% CI=1.5-9.1]; women who were ever in foster care [aOR=3.0; 95% CI=1.8-4.9] compared to women who were not. Non-significant covariates in the multivariable model included age, education, incarceration, injection drug use and duration of HIV.

Conclusions: Coercive sex is a significant yet under-considered risk factor and mode of HIV acquisition among women with HIV. Given the high rates of coercive sex as a mode of HIV acquisition (16.5% in our cohort), it should be considered a distinct HIV risk factor.

EPH2.8

The impact of food insecurity on sexual HIV risk negotiation with clients among youth sex workers in Metro Vancouver, Canada

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Background: Food insecurity is associated with heightened vulnerability to HIV/sexually transmitted infections (STIs) and reduced access to HIV/STI care. Much of this research has been conducted in resource-poor countries with limited data from resource-rich settings, despite evidence that food insecurity affects populations such as youth and sex workers (SWs). The objective was to determine the effect of food insecurity on sexual HIV risk negotiation with clients among youth sex workers (YSWs) aged 14-29 years in Metro Vancouver, Canada.

Methods: Longitudinal data (baseline and six bi-annual follow-up questionnaires) was drawn from An Evaluation of Sex Workers' Health Access ("AESHA"), a prospective community cohort of 723 street and off-street SWs between January 2010 and August 2013. SWs are recruited through street, indoor and online outreach to sex work venues. Bivariate and multivariable generalized estimating equations (GEE) logistic regression was used to examine the independent effect of measures of food insecurity (e.g. modified Radimer-Cornell food insecurity scale; such as food-related financial concerns and exchanging sex directly for food) and client condom refusal, an HIV risk indicator.

Results: Of 220 YSWs, 34.5% (n=76) reported client condom refusal over the 3.5-year study period, with 67.3% (n=148), 72.3% (n=159) and 13.6% (n=30) reporting inability to afford food, concerns about food running out, and exchanging sex directly for food, respectively over the study period, and 76.4% (n=168) reporting any type of food insecurity. In multivariable analysis, after adjusting for other HIV risk pathways, financial food insecurity remained positively associated with client condom refusal (AOR: 2.19, 95% CI: 1.28-3.74).

Conclusions: Three-quarters of YSWs experienced some kind of food insecurity and one-third reported client condom refusal. This study suggests a critical relationship between food insecurity and HIV/STI risk, indicating YSWs' acute vulnerability. Public food assistance should be implemented as a harm reduction measure with a focus on marginalized youth.

Social Sciences: Innovative Approaches and Outcomes in Social Science HIV Research

Sciences sociales : Recherches sur le VIH en sciences sociales : Approches et résultats innovateurs

SS2.1

Are public testimonials effective in fighting stigma? Lessons learned from a community-based evaluation project in Québec

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Background: Community-based organizations in Québec and elsewhere frequently use public testimonials in the fight against stigma and in order to raise awareness about the reality of people living with HIV/AIDS (PHAs). The main objective of the community-based research project "Partnership to evaluate the impact of public testimonials by people living with HIV" is to assess the effectiveness of testimonials by PHAs as a strategy for social intervention.

Method: The project is guided by a participatory action-research approach, the GIPA principle, and the principles of community-based research and implements the following method: 1) establishment of a working committee comprising representatives of community-based organizations, PHAs expert in public testimonials and academic researchers; 2) implementation of a database to make available an existing archive of testimonials; 3) selection of a sample of testimonials from the archive; 4) development of a preliminary evaluation grid measuring the impact of testimonials; 5) validation of the grid by the working committee with examples from the archive; 6) development of a final evaluative framework and 7) documentation and evaluation of this process.

Results: The evaluative framework was tested during events organized with different audiences. The results of these activities helped to assess the overall feasibility of this evaluation as well as specific issues. Impact was measured according to a set of indicators relative to three themes (HIV knowledge, attitudes towards PHAs, solidarity and potential for engagement). The evaluation of the research process itself sheds light on community capacity building, inclusiveness and democratic participation.

Next steps: The tools developed are being translated into English in order to scale up this work in other Canadian contexts. The project will enter a new stage to cover a wider range of modalities of testimonials and to include research into longer term impacts.

SS2.2

Transforming Interlocking Stigmas To Understanding, Compassion, and Hope: Critical Insights from CHAMP

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Background: HIV stigma is a major barrier to effective HIV response. Further, HIV stigma cannot be adequately addressed as an isolated phenomenon. Evidence suggests that HIV stigma can both be an extension of as well as a perpetuating factor for other types of stigmas and discrimination including homophobia, sexism, racism, socioeconomic marginalization, and xenophobia. While these interlocking stigmas pose challenges for HIV stigma reduction, effective strategies can be developed to use them as catalysts for critical dialogue and change.

Methods: CHAMP was a community-based intervention study (2011-2015) undertaken to reduce HIV stigma in the African, Caribbean, Asian and Latino communities in Toronto. The study tested the effectiveness of two interventions: Acceptance and Commitment Training (ACT) to promote psychological flexibility and Social Justice Capacity Building (SJCB) to promote collective empowerment for social action. All participants took part in SJCB and half of them also took part in ACT. This presentation will focus on distilling our data to identify key processes through which the two interventions operate.

Results: A total of 35 PLWHIV and 31 community leaders completed the interventions. Pre, post, and 9-month post-intervention quantitative data confirmed that ACT and SJCB reduced HIV stigma. Furthermore, our qualitative data showed that experiential learning activities designed specifically for CHAMP (e.g., Stigma Sculpture; Exclusion/Inclusion Circle) enhanced stigma reduction and collective empowerment. Analysis of the data indicated that these exercises: (1) increased participants' awareness and understanding of their unique and common experiences of marginalization and the power relations behind interlocking oppressions; (2) promoted empathy and compassion for self and others; and (3) inspired hope and commitment for social change.

Conclusion: Interventions to address HIV stigma must consider strategies that contextualize and tackle interlocking social stigmas and discrimination. Learning activities that promote mutual understanding, compassion, and hope contribute to emancipatory action.

SS2.3

HAART in Art: Historical Reflections on Artwork, Corporeality, and HIV Treatment Adherence

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With the persuasive focus on retooling HIV treatment for prevention, this presentation describes the changing relationship people living with HIV/AIDS have to HIV treatment. Through a historical analysis of the works of positive artists, I highlight themes arising with the release of highly active anti-retroviral therapy (HAART) and what these representations say about people's relationships to their bodies. I consider their critiques of medication and trace the differences between artistic representations of HAART in the late 1990s to the present as pharmaceutical and biomedical technologies emerge. I ask, in this new HAART panacea era—steeped in HIV criminalization, intensified surveillance, hyper-medicalization of prevention, and neoliberalization—how is medication represented in art created by people who often are targets of HIV treatment adherence practices? I examine surrogate markers of HAART adherence, namely the representations of viral load highlighting how surveillance is incorporated into corporeality. Affirming the persistence of AIDS activism, this paper offers a renewed commitment to cultural and political medicalization critiques of HIV in social science and humanities scholarship. Positive artists articulate not only the (un)fulfilled desire of treatment, but much more nuanced relationships, which include hope, promise, suspicion, disdain, resentment, hardship, critique, obsession, resistance, and tenacity.

SS2.4

Multi-Pronged Approach to Promote Integrative Knowledge Translation of Effective HIV Stigma Reduction Interventions

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Background: HIV stigma undermines HIV prevention, testing, and care. Unfortunately, resources and commitment to implement evidence-based stigma reduction strategies and interventions as policies, programs, and practice remain severely limited. To address this, the Community Champions HIV Advocates Mobilization Project (CHAMP) developed an approach to ensure that knowledge generated from the study is translated and applied in community practice.

Methods: CHAMP was a community-based intervention study (2011-2015) undertaken to reduce HIV stigma in the African, Caribbean, Asian and Latino communities in Toronto. Study results show that CHAMP interventions (Acceptance Commitment Training and Social Justice Capacity Building) were effective in reducing HIV stigma and mobilizing community action. To enhance knowledge uptake, we used a 4-pronged integrated knowledge translation (iKT) approach: (1) disseminating knowledge through community reports, conference presentations, and academic journals; (2) developing participant-driven knowledge translation initiatives to consolidate and sustain community engagement; (3) integrating intervention principles into existing or emerging community health promotion programs; and (4) developing knowledge-to-action research funding proposal to replicate and scale up the interventions.

Results: Our multi-pronged iKT enabled ongoing meaningful engagement of participants and agency partners, leading to successful dissemination and uptake of knowledge and resulting in: (1) over 50 community and academic abstracts, journals and presentations to various stakeholder groups; (2) four participant driven initiatives that included an anti-HIV stigma video production, a new PHA support group, a coalition to advocate on social justice issues and a project on HIV and aging; (3) adaptation and integration of CHAMP interventions into programs by partner agencies to address mental health and addiction, homophobia, racism and xenophobia; and (4) formation of an expanded cross-sector partnership to co-sponsor new knowledge to action research funding proposal.

Conclusion: Multi-pronged stakeholder-driven iKT strengthens community engagement. It builds equitable partnerships that support the integration of evidence-informed HIV stigma reduction strategies into frontline practices.

SS2.5

Presenting research as visual narrative: Representing Black men, masculinity and HIV in "The Test"

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Health promotion strategies challenge people to think seriously about their health, encourage critical dialogue on health-related practices and behaviours, and support people to adopt life-enhancing practices. But can health promotion actually make people re-evaluate concepts and practices deeply engrained and understood as commonsense? Can health promotion practitioners induce people

to interrogate the "normal" in their lives without making them feel abnormal in the process?

This presentation critically appraises health and health promotion through *"The Test"* (2015), a short film that we developed as a KTE initiative from the *iSpeak* research study that was implemented in 2011-2013. *iSpeak* explored the HIV-related needs, challenges and priorities of heterosexual Black men in Ontario through (a) focus groups with HIV-positive and HIV-negative self-identified heterosexual Black men in Toronto and London, (b) a focus group with community-based service providers who work with Black communities in Ontario, and (c) one-on-one interviews with researchers who work on health-related issues among Black communities.

"The Test" dramatizes the sense of vulnerability associated with getting tested for HIV. Contrary to the pathological stereotypes associated with Black men, the film draws on *iSpeak* to demonstrate Black men's agency in relation to their health and wellbeing. Based on the visual narrative, we illustrate and discuss the links between men's health practices and the social and cultural contexts that shape masculinity and other aspects of male self-making. We query the politics of representing race, gender and sexuality in HIV-related health promotion, and discuss the role of anti-racist and anti-oppression frameworks in making HIV prevention more meaningful and transformative. Finally, drawing on our experience showing the film to diverse audiences, we discuss contradictory reactions to the film, and perspectives on how the film may inspire and support discussion around the meaning and significance of manhood and masculinity in men's health and HIV-related health promotion.

SS2.6

HIV Criminalization: Racialization, Immigration and the Media

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In Canada, concerns have been raised that media reporting of HIV non-disclosure criminal cases is sensationalist, fuels racist stereotypes that link Black men with criminality, exaggerates the risk of HIV transmission, and contributes to public fears about racialized immigrants living with HIV. Despite the prominence of these concerns in political and research discourses about HIV criminalization, until this time there has been no comprehensive analysis of Canadian media coverage of such cases. This paper reports on findings from a study funded by the CIHR SRC in HIV Prevention that responds to this gap in knowledge.

This study aimed to provide: 1) a stable empirical foundation for settling claims about the potential overrepresentation of racialized defendants in mainstream media coverage of HIV criminal non-disclosure cases; 2) a rigorous analysis of key strategies of representation used to frame media coverage of HIV criminalization.

To meet these objectives we systematically searched the Factiva database for newspaper coverage of Canadian HIV non-disclosure criminal cases from 1989 to 2015 and identified a corpus of 1744 articles. The paper reports quantitative findings that support claims about overrepresentation. For example, racialized immigrants represent 22% of known Canadian defendants but are the focus of over 60% of the articles in our corpus. Four cases involving Black immigrant men living with HIV account for over half of all the newspaper coverage. Drawing on classic work on cultural representation, racialization, crime, and othering (Hall 1997) we identify three strategies critical to "the regime of representation" that constitute Black immigrant men as idealized perpetrators of HIV-related sex crimes: telling stories in criminal justice time; constituting hypersexual, amoral subjects; and representing the men as non-Canadian, "African others." Our study confirms community concerns that racialized immigrants are overrepresented in media coverage and identifies problematic forms of representation to be critiqued and remade.

SS2.7

Number of Psychosocial Strengths Predicts Reduced HIV Sexual Risk Behaviours Above and Beyond Syndemic Problems Among Gay and Bisexual Men

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Background: Syndemics research has shown that the additive effects of multiple psychosocial problems is associated with high-risk sexual behavior among gay and bisexual men. Similarly, psychosocial strengths, such as coping behaviors, may play a protective role against high-risk sexual behavior despite the presence of syndemic psychosocial problems. We hypothesized that the number of psychosocial strengths would predict lower likelihood of condomless anal sex (CAS) with serodiscordant (HIV-positive or unknown HIV status) partners, despite the number of syndemic problems.

Methods: In a 3-timepoint study of 470 HIV-negative gay and bisexual men, we examined how syndemic problems and psychosocial strengths predict CAS with serodiscordant partners. Regression models were computed with psychosocial problems at baseline, number of psychosocial strengths at T2, and CAS with serodiscordant partners at T3, measured 3 months apart. Mediation using bootstrapping was used to detect indirect effects of psychosocial problems on CAS with serodiscordant partners.

Results: At T3, participants reported a mean of 6.62 sexual partners in the past 3 months, and 34% reported CAS with serodiscordant partners. The number of psychosocial

problems was associated with CAS with serodiscordant partners, RR=1.32, 95% CI =1.02-1.70. However, when adding the number of psychosocial strengths to the model, the effect of psychosocial problems was no longer significant, and the number of strengths-based factors remained significant, RR=0.86, 95% CI=0.74-1.00. We detected an indirect effect of psychosocial problems on CAS with serodiscordant partners, mediated by a lower number of psychosocial strengths, β=0.04, 95% CI=0.002-0.09.

Conclusion: These findings are the first showing the benefits of examining psychosocial strengths in models of sexual risk behaviours. Strengths-based factors predict reduced CAS with serodiscordant partners above and beyond risk factors typically assessed in the syndemics literature. In addition, syndemic psychosocial factors have their effects on CAS with serodiscordant partners via decreasing the protective effects of psychosocial strengths.

SS2.8

"More Than Fiction: Phase 2" - ASAAP Anthology Project for People Living with HIV/AIDS

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Background: The "More Than Fiction" project was developed to inspire research in narrative writing initiatives for people living with HIV/AIDS with a focus on therapeutic and social outcomes.

In 2014, ASAAP launched "More Than Fiction: POZ Women Share their Stories", a collection of twelve (12) personal narratives by South Asian women living with HIV. The print edition has been widely distributed and presented at a number of events including CAHR2015.

Due to its overwhelming success, in 2015, ASAAP adapted the anthology project to include South Asians living with HIV/AIDS from the agency's mixed-gender support program – Connecting to Care. "More Than Fiction: Phase 2" focuses on stories that address determinants of health: housing, employment, immigration, trauma, mental health, HIV stigma and discrimination. These stories also illustrate the unique and complex circumstances of the participants' lived experiences.

Method: Fifteen (15) participants for the project were recruited to attend workshops on storytelling and photo voice led by two (2) Peer Facilitators. The Peer Facilitators were invited from the group of POZ women who had participated in the 2014 edition of the anthology. After the Peer Facilitators received training in group facilitation, they presented eight (8) workshops from August to October (2015). Focus groups will be organized following the anthology's launch.

Results: "More Than Fiction: Phase 2" is expected to launch in early March 2016. An inclusive capacity-building approach that draws on the knowledge and experience of Peer Facilitators, participants, and project advisory members continue to inform the overall implementation and production of the publication.

Conclusion: ASAAP would like the opportunity to present and share with the greater HIV/AIDS service and research sectors its unique narrative writing model adapted for "More Than Fiction: Phase 2" to continue to foster positive change in service and support provision.

Multi-Disciplinary: PrEP and Other Novel HIV Prevention Strategies

Multidisciplinaire : PrEP/PPE et autres nouvelles stratégies de prévention du VIH

MD1.1

High adherence but modest risk compensation among MSM in a PrEP demonstration project

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Background: PrEP is highly efficacious at preventing HIV, but concerns persist about adherence and increased sexual risk-taking ('risk compensation'). We present preliminary findings on these outcomes from PREPARATORY-5, Canada's first PrEP demonstration project.

Methods: HIV-uninfected adult MSM scoring ≥10 on a validated HIV risk score (HIRI-MSM) and reporting condomless receptive sex in the preceding 6 months were enrolled into a one-year, open-label clinical trial of daily tenofovir/emtricitabine. Visits occurred at baseline, 1, 3, 6, 9 and 12 months, and included adherence assessments (pill count, four-day recall), sexual behaviour questionnaires (last 6 months), and laboratory testing for HIV, STIs and renal function.

Results: 52/90 men screened met eligibility criteria and were enrolled; 83.7% of visits are complete. Participants were mostly white (73.1%), young (median age 33, IQR=28,37), gay (94.2%) men taking no prescription medications (IQR 0,1) and one supplement (IQR 0,3) at baseline. Most (69.2%) had a history or baseline diagnosis of ≥1 bacterial STI. Median overall adherence was high at 98.4% (96.2%,100%) by pill count, and adherence four-day recall was perfect at 89.7% of visits. Between baseline and month 9, there was no significant change in median number of

partners (18 vs 15, Wilcoxon signed rank p=0.81), or condomless receptive anal sex acts (5 vs 7.5, p=0.49), but HIV+ partners increased from 1 (IQR=0,3) to 2 (IQR=1,7, p=0.02) and condomless anal sex acts with HIV+ partners rose from 0 (IQR=0,4) to 6 (IQR=1,15, p=0.001). Many (24/52, 46.2%) participants experienced ≥1 incident bacterial STI, including 4, 13, 19 and 4 episodes of syphilis, gonorrhea, chlamydia/non-specific urethritis and LGV respectively. No HIV seroconversions occurred. There was one creatinine elevation beyond grade 2, which resolved spontaneously.

Conclusions: Despite frequent STIs, PrEP has been associated with high adherence and no HIV infections in this MSM demonstration project. Modest risk compensation occurred with HIV+ partners.

MD1.2

Importance of Recruitment Process and Epidemic Initiation in Mathematical Models for Evaluating HIV Prevention Interventions

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Mathematical models are invaluable tools in evaluating the potential benefits of different HIV prevention programs. Demographic processes, not being directly related to the intervention and assumptions on initial epidemic state are often neglected and rarely justified. Our goal is to investigate how some of these conditions affect the evaluation of HIV prevention interventions.

We modified a dynamical mathematical model of HIV transmission from the literature. We explored different mechanisms for recruiting individuals into the population, and different procedures for initializing the epidemic at the start of preventive intervention. Across simulations, we compared the projected course of the epidemic over 20 years by estimating the population size, the HIV prevalence and the number of HIV infections prevented by the intervention.

We found that recruitment and initiation assumptions strongly affect the epidemic statistics (see Table). Seeding the epidemic at intervention initiation results in less than 10% differences in epidemic statistics after 20 years. Letting the epidemic stabilize before commencing the intervention results in distinct states depending on the recruitment process. Thus, carrying an incorrect recruitment process over time before starting an intervention may invalidate its evaluation of the number of infections prevented.

These results suggest that recruitment processes and epidemic initiation play a critical role when HIV prevention interventions are evaluated using mathematical models. These assumptions should be carefully examined and justified. In particular, impact projections of interventions that can only be initiated in the future (e.g. due to ongoing development) must be interpreted with caution due to the uncertainties we investigated.

Epidemic statistics after simulating 20 years of HIV prevention intervention (50% coverage, 70% efficacy)

Cell format: Mean (Min – Max) for Population size (thousands) HIV prevalence # infections prevented (thousands)		**Recruitment process** r(t) : rate of individuals entering the population at time t N(t) : population size at time t M : maximal population size (logistic only)			
		Constant r(t) = c (a constant)	Linear r(t) proportional to N(t)	Delayed linear r(t) proportional to N(t-15)	Logistic r(t) proportional to N*(M-N)
Epidemic initiation	Intervention start with seeded epidemic	1734 (1697–1762) 6.2% (5.1%–7.2%) 346 (287–418)	1603 (1544–1645) 6.6% (5.5%–7.7%) 341 (284–410)	1722 (1682–1752) 6.2% (5.1%–7.3%) 346 (287–417)	1721 (1680–1752) 6.2% (5.1%–7.3%) 345 (287–417)
	Intervention start at HIV equilibrium	1910 (1844–1950) 0.6% (0.3%–1.4%) 48 (22–94)	315 (180–576) 1.7% (0.8%–3.7%) 18 (14–24)	740 (570–989) 1.1% (0.6%–2.5%) 31 (18–49)	1896 (1815–1945 0.6% (0.3%–1.4%) 47 (21–91

MD1.3

PrEP in Montreal: Good Adherence, No Seroconversion and No Evidence of Risk Compensation

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Background: This study presents the real-life PrEP experience in Canada evaluating treatment uptake, adherence and behavioral changes.

Methods: We prospectively assessed patients receiving PrEP (TDF-FTC) at Clinique médicale l'Actuel. Patients were seen at baseline and at 3-month follow-up intervals (FU). Treatment adherence and behavioral data (condom use and number of sexual partners) were measured by self-report at every FU and analyzed by c^2.

Results: 355 patients were included. The main indication for PrEP was regular unprotected anal intercourse (69%), repeated use of PEP (14%) or couples in sero-discordant relationships (14%). Patients requesting PrEP were male (99%) and MSM (97%) with a median age of 36 (range=18-66y). 80% had a history of STIs and 73% had >10 sexual partners in the last 12 months. Mean condom use was 49% for receptive anal intercourse and 48% for insertive. In 69% of cases TDF-FTC was taken die (adherence problems=4%). Mean duration of PrEP was 6.5 months, no seroconversion was observed. 49 patients (21%) stopped PrEP with 49% of treatment discontinuations arising in the first 3 months: 39% due to 'no longer need,' 23% for adverse events. High-risk behavior (p=0.018; see Table 1) at 3-month FU, saw

25% increase, 43% no change and 32% decrease. Patients with improved behavior were those that were most at risk of HIV.

Conclusions: Patients receiving PrEP were at high risk for HIV and seem adherent to treatment and to follow-up. No seroconversion occurred. In short term, PrEP does not promote an increase in high-risk behaviors.

	Inconsistent condom use at BL (<80%)	Regular condom use at BL (>80%)	Total
Worsening behavior (less condom use, more partners)	15 (24%)	17 (27%)	32 (25%)
No change (no change in condom use or no.partners)	21 (33%)	34 (53%)	55 (43%)
Improved behavior (more condom use, fewer partners)	27 (43%)	13 (20%)	40 (32%)
Total	63 (100%)	64 (100%)	127 (100%)

MD1.4

KONTAK: a service offered to guys who f*** other guys. You demand…..we supply !

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Résumé :

This talk is to enlighten some of the key factors that contributed to the success of a project that aim to reach a key population (MSM attending sex parties) in regards to STBI prevention.

Sex can be nasty business! We want you to have the good kind of nasty, so we provide everything you need for your sex party and we deliver it right to your door.

Kontak is a project developed by ACCM (AIDS Community Care Montreal), a volunteer-based community organization working to enhance the quality of life of people living with HIV/AIDS, as well as to prevent HIV and other STBBI's transmission, and to promote community awareness and action.

Kontak is a sexual health initiative that aims to lower STBI transmission by delivering safer sex supplies (condoms, lubricants, latex gloves etc.), pamphlets, and wholesale priced sex toys to organizers and participants of gay and mixed-orientation sex parties in the region of Montreal. A Kontak outreach worker also facilitates risk reduction and safer sex information sessions at parties, and is present to answer sex-related questions in a non-judgmental manner. It's by this non-judgemental approach and by being very accessible through various ways that Kontak developped, in about two years, a successful approach to reaching out a key population in regards of STBI prevention.

This innovative program is financially supported by the Public Health Department of Montreal. Services and interventions are available in French and English, during the week including weekends, day or night.

Kontak website contains sexual health testimonials from sex party participants, safer sex information, and links to sexual health resources and support, as well as menus and ordering details for sex supplies.

http://accmontreal.org/education-prevention/projects/kontact/

For more information, or to place an order, e-mail us at outreach@accmontreal.org or text 514-941-SEXE (7393)

http://accmkontak.com/

MD1.5

Rectal 1% Tenofovir Gel use Modulates Epidermal Protein Expression

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Rectal use of 1% Tenofovir (TFV) gel is being explored as an HIV prevention option for men who have sex with men and other high risk groups, and requires assessment of mucosal safety and tolerability. Here we utilized a mass-spectrometry based proteomics approach to evaluate mucosal immune responses of participants using rectal TFV gel. Project Gel was a Phase 1 randomized, double-blind, multisite, placebo-controlled trial in which 24 participants were randomized 1:1 to receive rectal TFV or a hydroxyethyl cellulose (universal placebo or HEC) gel daily for 7 sequential days. Rectal secretions were collected at each visit using swabs and analyzed by label-free tandem-mass spectrometry with differential protein expression after 7 daily doses relative to a baseline (paired t-tests, $p<0.05$), and multivariate (LASSO) modelling. A significant decrease in epidermal barrier proteins was identified with 7 daily doses of TFV use that was not observed in samples from individuals in the HEC arm. Multivariate modelling identified 13 proteins that confidently separated TFV gel users from those in the HEC arm (100% calibration and 96% cross validation accuracy), and included the epithelial integrity factors (FLMNB, CRNN, CALM), serpins (SPB13, SPB5) and cytoskeletal proteins (VILI, VIME, WRD1). This study suggested that daily rectal applications of 1% TFV gel is associated with mucosal

proteome changes involved in epidermal development that may be important to assess in future TFV gel studies following prolonged exposure.

This study was funded by CIHR (OCB134115) and NIH (R01 HD059533).

MD1.6

Daily oral use of acetylsalicylic acid (ASA) reduces HIV target cells at the female genital tract

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Introduction: HIV incidence among female sex worker (FSWs) is very high. However, despite being at high risk a small group remains HIV uninfected. We have observed that HIV-exposed seronegative FSW have a unique immune phenotype called Immune Quiescence (IQ). IQ is a state of no inflammation where decreased levels of baseline cytokine/chemokines and low levels of T cell activation result in fewer HIV target cells in the female genital tract (FGT). We hypothesised that the anti-inflammatory agent acetylsalicylic acid (ASA) can induce the IQ phenotype and reduce HIV target cells.

Methods: Non-FSW HIV uninfected women from Kenya were enrolled and followed for three months. At month 1, systemic/mucosal baseline immune activation was assessed. Participants received 81mg of ASA daily and were followed for a 2 months period to assess T cell immune activation.

Results: Analysis showed that oral uptake of ASA (81mg/day) decreased the expression of CCR5 on CD4+ T cells (p=0.02) and decreased, by 14%, the frequency of CD4+CCR5+ (p=0.05) T cells in the blood. We also observed that the decrease of CD4+CCR5+ T cells in the blood was inversely proportional to the ASA level in the blood. The analysis of the cervico-vaginal lavage and plasma demonstrated that after uptake of ASA there is a modification in the chemokine gradient. More importantly, this study showed that oral administration of low dose ASA decreased by 40% the frequency of HIV target cells (CD4+CCR5+ T cells) at the female genital tract.

Conclusion: ASA is an affordable and worldwide available anti-inflammatory agent. Daily oral administration of low lose ASA resulted in significant decreases in the number of HIV target cells in the FGT. Therefore, daily uptake of ASA could represent a new avenue to prevent HIV infection, which would be affordable for the most vulnerable populations and not associated with any stigma.

Multi-Disciplinary: HIV in Indigenous and Local Populations

Multidisciplinaire : Le VIH dans les populations autochtones et locales

MD2.1

Antiretroviral drug resistance among people experiencing treatment interruption in rural regions of British Columbia

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Introduction: Geographic disparities in health have been well documented in rural Canada. However, data evaluating HIV-related health outcomes among rural populations in Canada is limited. This study compared rates of antiretroviral (ARV) drug resistance between rural and urban individuals who experienced ≥1 ARV treatment interruption (TI).

Methods: This retrospective analysis included individuals (≥19 years) who initiated ARV therapy between 2000 and 2014 through the BC Drug Treatment Program. Participants had at least one TI >90 days, virologic rebound following TI and no documented ARV resistance at first ARV initiation. Rurality was defined by General Practice Rurality Index (GPRI). Resistance was determined by genotypic HIV testing. Poisson models were used to assess rates of ARV resistance.

Results: Of 192 individuals included in the analysis, 171(89.1%) had a GPRI 0-10, 15(7.8%) had a GPRI 11-30 and 6(3.1%) had a GPRI >30. GPRI >30 was associated with increased risk of ARV resistance compared to GPRI 0-10 (RR 10.22, 95% CI: [3.59-29.08]). Among participants with GPRI >30, 2(33.3%) had no resistance, 3(50.0%) had resistance to one ARV class and 1(16.7%) had resistance to two classes. Among participants with GPRI 0-10, 142(83.0%) had no resistance, 15(8.8%) had resistance to one class, 10(5.8%) had resistance to two classes and 4(2.3%) had resistance to three classes. No significant differences were observed between rates of ARV resistance in rural and urban areas in additional analyses when rurality was defined by postal code or Statistical Area Classification.

Conclusion: Individuals living in rural regions of British Columbia may be at increased risk of ARV resistance following a TI. However, this study was limited by a small number of participants in rural regions and further research is needed to evaluate the impact of TI on ARV resistance among people living with HIV in rural areas.

MD2.2

A Community Needs Assessment with Indigenous Peoples Living with HIV/AIDS in Saskatoon, Saskatchewan

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Saskatoon has nearly half of the diagnoses of HIV in the province, with an incidence rate among Indigenous populations that is two to three times higher than the national rate. Previous research in Saskatoon, and across Canada, has found that inequities exist in the amount and type of access to healthcare that Indigenous Peoples living with HIV/AIDS (IPHA) receive compared to the general population; leading to greater risk for HIV transmission, less access to treatment, and more complex health issues leading to poorer health outcomes. Generalized approaches to HIV prevention and treatment, however, have been less effective with Indigenous populations than with non-Indigenous populations. By working with Indigenous community members to define and outline health service needs, this research can inform, support, and improve services provided to the IPHA population. This project conducted a community needs assessments regarding the lived experiences and health concerns of IPHA in Saskatoon, including their health service needs, gaps and barriers to treatment, and community stakeholders' perspectives. Community needs assessment is a qualitative data collection process that develops an evidenced-based understanding of the health needs of a target population related to multiple determinants of health. Our research has involved over 30 semi-structured interviews with IPHA in Saskatoon, both male and female. This paper will focus on the key themes that emerged from the community needs assessment methodology. By examining and seeking community input on how to address structural, societal, and personal obstacles, upstream interventions can be developed to build local service capacity through improved resource utilization, better health education, and new affirmative health services for IPHA in Saskatoon and in other urban contexts across Canada.

MD2.3

The Cedar Project: Longitudinal health outcomes associated with childhood physical and sexual abuse among young Indigenous people who use drugs in BC

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Background: Indigenous leaders are concerned that historical/lifetime traumas contribute to HIV/HCV epidemics among their young people. Few studies have explored the effects of childhood physical abuse (PA) and sexual abuse (SA) on HIV risk among young Indigenous people who use drugs.

Methods: The Cedar Project is a cohort of young Indigenous people (14-30) who use drugs in Vancouver, Prince George, and Chase, BC. The Childhood Trauma Questionnaire (CTQ) determined experience and severity (none; low/moderate; severe) of childhood PA and SA. Generalized mixed effects models explored associations between severity of PA and SA with HIV risk between 2003-2012.

Results: Overall, 266 participants (53% women; mean age 23 years) completed the CTQ and at least one follow-up. For PA, 39.8% reported none, 16.5% reported low/moderate, and 41.4% reported severe levels. For SA, 41% reported none, 16.9% reported low/moderate, and 38.7% reported severe levels. Severe SA was associated with having a parent who had attended residential school (p=0.002). In multivariate analyses, an increase of one level of PA severity was associated with homelessness (AOR: 1.27; 95%CI: 1.01-1.59); binge drinking (AOR: 1.31; 95%CI: 1.02-1.70); sex work involvement (AOR: 1.5; 95%CI: 0.95-2.37); inconsistent condom use (AOR: 1.74; 95% CI: 1.21-2.50); sexual assault (AOR: 1.53; 95%CI: 1.05-2.22); high frequency cocaine injection (AOR: 1.37; 95%CI: 0.97-1.92); and binge injection (AOR: 1.7; 95%CI: 1.26-2.31). A one level increase of SA severity was associated with sex work (AOR: 2.0; 95%CI: 1.29-3.22); inconsistent condom use (AOR: 1.58; 95% CI: 1.08-2.32); sexual assault (AOR: 1.5; 95%CI: 0.99-2.29); high frequency cocaine injection (AOR: 1.67; 95%CI: 1.16-2.40); binge injection (AOR: 1.58; 95%CI: 1.16-2.13); and HCV infection (AOR: 3.5; 95%CI: 1.65-7.24).

Conclusion: Childhood abuse experiences profoundly impact the health of Indigenous people throughout their lives. The urgent need to develop public health responses that recognize both profound grief and cultural strengths cannot be overstated.

MD2.4

Developing Women-Centered HIV/AIDS Services in Manitoba: A Community-Based Participatory Research Study

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1. University of Manitoba, Winnipeg, MB 2. Ka Ni Kanichihk, Winnipeg, MB 3. Nine Circles, Winnipeg, MB 4. 595 Prevention Team, Winnipeg, MB

Aboriginal (First Nations, Metis, Inuit) and allied partners in Manitoba (Ka Ni Kanichihk, 595 Prevention Team, Nine Circles Community Health Centre, Manitoba HIV Program and the University of Manitoba) have come together to understand and address care needs of Manitoba First Nations, Metis and Inuit women with HIV/AIDS. This project is part of a larger national cohort study that aims to implement and assess the effect of women-centered HIV/AIDS services (Canadian HIV Women's Sexual and Reproductive Health Cohort Study – CHIWOS). Goals of the nascent Manitoba project are to: 1) identify strengths and gaps associated with current HIV care and support for First Nations, Metis and Inuit women, as described by First Nations, Metis and Inuit women and those who work with them; 2) support efforts to identify, communicate and document recommendations on how to best resolve care and support gaps; and 3) engage in knowledge synthesis and exchange. The project is grounded in community-based research methods. First Nations, Metis and Inuit women are at the center of this project and along with their children and family will be respected and honoured. Advisory Groups are being formed to guide all aspects of the project. The specific research objectives for this project will be developed with HIV positive First Nations, Metis and Inuit women in Manitoba. Our presentation will include a description of the epidemiology and impact of HIV/AIDS on First Nations, Metis and Inuit women in Manitoba, HIV/AIDS services for women in Manitoba, the history of the research project and progress to date including the formation and continuing development of the research partnership.

MD2.5

High Mortality Rates in HIV-Positive Individuals from Southern Saskatchewan - A Comparative Analysis Between Two Canadian Prairie Clinics

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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. We characterized mortality in our Regina-based cohort within the HIV treatment cascade and examined baseline predictors of mortality to determine appropriate and necessary program and public health interventions. We compared our results with those from the neighbouring Southern Alberta Clinic (SAC) in Calgary, Alberta.

Methods: This retrospective study included all individuals with a first confirmed positive HIV test in the Regina Qu'Appelle Health Region (RQHR) between January 1, 2006 and July 1, 2015. Cases were reviewed to determine baseline characteristics, cause of death, and to place deaths within the HIV treatment cascade. Logistic regression was used to examine factors associated with a higher risk of mortality.

Results: 351 newly-diagnosed individuals in RQHR were included, 60 of whom died. The overall all-cause mortality rate was 5.1 per 100 person-years, 3.4 times greater than the mortality rate of 1.5 per 100 person-years at SAC. A high proportion of deaths occurred prior to linkage to care (17/60, 28%), or after linkage but before retention in care (23/60, 39%). Baseline characteristics which predicted an increased risk of mortality included age > 35 years (OR 4.46; $p<0.001$), injection drug use as primary risk for acquisition of HIV (OR 2.10; $p=0.043$), and Indigenous ethnicity (OR 2.43; $p=0.008$).

Conclusions: HIV-positive individuals in RQHR have an all-cause mortality rate 3.4 times greater than SAC. Over two-thirds of deaths occurred in those either not linked or retained in care, and those with HIV at greatest risk of death in our cohort are older Indigenous individuals with a history of injection drug use. Urgent interventions to target those at greatest risk of mortality and to improve the early HIV treatment cascade in RQHR are required.

MD2.6

HIV Transmission Networks in the Province of Saskatchewan

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HIV transmission is often difficult to analyse due to unreported pattern and stigmatization of risk behaviours within social or sexual networks. Understanding HIV transmission dynamics is important for planning and evaluation of effective prevention interventions. Recent advances in molecular epidemiology have made it possible to reconstruct HIV transmission networks using drug resistance genotype data. HIV drug resistance testing is recommended in persons with

HIV infection at entry into care regardless of whether antiretroviral therapy will be initiated immediately or deferred.

Methods: HIV genotyping was conducted on specimens submitted to the Canadian HIV Strain and Drug Resistance Surveillance Program from treatment-naive individuals newly diagnosed with HIV in Saskatchewan from 2004 to 2011. Transmission cluster analysis utilising HIV sequence, demographic, and geographic data was performed to infer putative transmission patterns. Correlates of identified clusters were analyzed and spatiotemporal relationships were explored.

Results: Following quality filtering, of 784 HIV pol sequences analyzed, 602 (77.6%) were involved in 41 clusters ranging from 2 to 128 individuals. Cluster formation was heavily associated with geographic region. For example, 444 of the apparent transmission events (71%) formed three large clusters significantly associated with individuals from one of three health regions respectively. While the greatest degree of inter-regional transmissions were observed between these three regions (n = 131), transmissions between urban and rural settings were also observed (n = 46).

Conclusions: Construction of HIV transmission networks is a valuable tool to enhance HIV surveillance and monitoring efforts. Timely identification and investigation of clusters can inform focused prevention interventions. Effective use of HIV drug resistance genotype data for public health action will require revising information flows of the current provincial surveillance system building upon recommended clinical laboratory testing practices.

Multi-Disciplinary: HIV in the Global Context

Multidisciplinaire : Le VIH dans le contexte mondial

MD3.1

Social Construction of HIV/AIDS in an Indigenous population in Colombia

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During the last 15 years the number of Indigenous people with HIV/AIDS has increased in countries such as Canada, United States, Mexico, Brazil, and Colombia. UNAIDS documents that in 2014 there were 37 million people living with HIV in the world and in that same year 1.2 million died, and that there was an incidence of 2 million people. In Colombia the estimated prevalence in the general population is 0.52%, without specific information in relation to Indigenous peoples. A 2010-2013 study by the Universidad de Antioquia suggested a prevalence of 1% among the Embera Chami community of Cristiania, Antioquia, and of 0.5% among Wayuu communities of Maicao, La Guajira. Despite constitutional rights recognized in 1991 for Indigenous peoples in Colombia, there are still significant vulnerability issues among Indigenous communities that impact health status.

Between 2012 and 2014 researchers of this community-based study conducted interviews, focus groups, and documented contextual information to better understand the perceptions and social responses among Wayuu communities in relation to risk HIV transmission. The data was analyzed from a social construction perspective. Men and women 16 years of age and older participated in the study. The study was done with the approval and support of the Wayuu Authorities and Indigenous health organizations. The data was gathered in the Indigenous language (Wayuunaiki) and translated to Spanish by an Indigenous working group for the purposes of analysis.

The findings suggested that HIV/AIDS is seen as an illness that is not of earth or wind, and that stands in opposition to cultural principles given its association with non-Indigenous life. The study helped understand the ethnic and gender view of HIV/AIDS among the Wayuu, as well as other Indigenous communities in the region.

MD3.2

Predictors and evolution of antiretroviral therapy adherence among HIV-infected adolescents in Brazil: results from a one-year longitudinal study

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Background: Optimal adherence to antiretroviral therapy (ART) is a challenge for many people living with HIV, especially adolescents. Medication adherence is a complex phenomenon influenced by multiple factors.

Objective: To examine the evolution and predictors of medication adherence among perinatally infected youths (PIY) in Sao Paulo, Brazil.

Methods: During a one-year longitudinal cohort study, PIY taking ART aged 13-21 were recruited in hospitals and HIV/AIDS reference centers; data were collected at baseline (T0) and after 12 months (T1). Adherence was defined as taking ≥ 95% of prescribed HIV medication in the past 7 days. Analysis of variance (ANOVA) and generalized estimating equation (GEE) methods were used and statistically significant results at $p \leq .05$ are presented.

Results: From 05/2011 to 03/2012, 268 adolescents enrolled in the study (59% female; mean age of 16 years). At baseline, 63.6% of the sample was adherent to their HIV medication and 52.99% had an undetectable viral load.

Participants reported: low levels of stress and symptoms of depression; high perception of self-efficacy and social support; a mean of 6.8 symptoms related to their HIV medication. Between baseline and follow-up, 49.6% remained adherent (A/A) and 22.3% remained non adherent (NA/NA). ANOVA results indicated that, compared to A/A, NA/NA showed more symptoms related to HIV medication and were more incommoded by them. NA/NA were more stressed and depressed. They also had a lower perception of their self-efficacy. In the final GEE model, predictors of adherence were: high perception of self-efficacy [OR: 2.81; 95% CI: 1.94–4.05] and low number of reported medication side-effects [OR: 0.97; 95% CI: 0.95–0.99].

Conclusion: Only half of the youth in this sample remained adherent to their HIV medication over one year. These findings suggest the need to develop interventions to enhance self-efficacy and to help youths better manage HIV medication side-effects.

MD3.3

Intervention fidelity, process evaluation and effectiveness of complex HIV prevention intervention for female sex workers in Bangladesh

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Background: Targeted interventions for female sex workers (FSWs) are often complex in nature and cannot always be implemented in full fidelity because contextual factors which may require adaptation. This study aims to assess intervention fidelity and implementation process in order to explain observed effect of the four-pronged targeted intervention for FSWs in Bangladesh.

Methodology: A quasi-experimental pre-test and post-test design study was conducted to understand the effect of changes planed in the programme in terms of i. Drop-in-centres (DIC) operations, ii. STI services provisions, iii. condom distribution methods and, iv. advocacy strategies. Data collection was done through baseline and endline surveys at 12 months apart form 614 FSWs in each phase from 4 intervention DICs and 4 comparison DICs in Dhaka city. Qualitative information was collected from in-depth interviews with 40 FSWs and 23 key informant interviews. Process implementation data was collected on monthly basis through monitoring of records and registers.

Results: Planned changes in programme were delayed between 3 to 6 months in the four intervention DICs. Only <50% of the FSWs were available at the endline survey of those who participated at baseline. Out of three primary outcomes (consistent use of condoms, having had symptoms of STIs and experience physical violence), significant difference in rate change of -14.34% was observed only in reported STI symptoms among the FSWs in the intervention group. Out of 12 secondary outcomes selected apriori, significant differences in rate change were observed in case of 'treatment completed' and 'partner card given from the DICs'.

Conclusions: Effectiveness of the intervention could not be ascertained either because of low adherence to intervention fidelity or saturation effect in some of the outcomes for example, reported high condom use at baseline in both the intervention and control group.

MD3.4

Low frequency AZT Drug Resistance in Ugandan Patients Failing ART with Susceptible HIV Sanger Genotyping

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Background: Previously we have described that despite close monitoring and adherence to treatment each year over 10% of patients fail first line treatment regimens (Kyeyune *et al* 2013 *AIDS* 27:1899). Within this cohort from the Joint Clinical Research Centre (JCRC) we identified a subset of patients failing treatment that were resistant to NNRTIs and FTC/3TC but lacked thymidine analog mutations (TAMs). It is likely that some of these patients are failing treatment due to the presence of low-level mutations that Sanger sequencing failed to detect.

Methods: We used two novel HIV-1 genotyping assays based on oligonucleotide ligation assay (OLA) and a deep sequencing assay (DEEPGEN™HIV) to quantify minority HIV-1 drug resistant variants. The assays were used on a cohort of 50 patients that by Sanger sequencing had NNRTI and FTC/3TC resistance but lacked thymidine analog mutations (TAMs).

Results: OLA identified low frequency TAMs in 60% (30/50) of these patients. A sub-set analyses using DEEPGEN™HIV confirmed the low frequency TAMs detected by OLA. For all 50 patients failing first line treatment but lacking dominant AZT resistance, the thymidine analog drug remained in the regimens leading to possible salvage treatment failure.

Conclusions: These low frequency drug resistant variants detected in antiretroviral-experienced individuals failing treatment, may have significant consequences on current or future outcomes, especially if treatment is not modified based on a susceptible HIV-1 genotype (Sanger) report. Preliminary data suggests that patients with minority drug resistance variants associated with treatment failure did not respond to the continuation of the same treatment regimen.

MD3.5

Integrin a4b7 expression on CD4+ T cells as a predictor of HIV acquisition and disease progression

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Gut inflammation is a hallmark of several human diseases including inflammatory bowel disease and HIV infection. The integrin α4β7 is critical for the homing of lymphocytes to the gut mucosa and gut associated lymphoid tissue. CD4+ T cells expressing high levels of α4β7 were shown to be the preferential targets of HIV/SIV infection. Increased frequencies of α4β7 expressing CD4+ T cells within GALT at the time of infection appear to correlate with increased VL and rate of disease progression post SIV infection. Here we study the CAPRISA 004 tenofovir trail PBMCs from a median of 110 days prior to infection to asses the role of β7 Integrin in HIV acquisition and disease progressions as well as profile CD4+ T cells in terms of their memory, activation, and target cell properties. Our results show that higher integrin β7-Hi expression on blood CD4+ T cells is associated with higher HIV acquisition rates independent of age and HSV2 serostatus. The pre-infection β7-Hi levels correlated significantly with increased VL (both peak and median) and more rapid rate of CD4 loss and a lower CD4:CD8 ratio. Together these data demonstrate an important role for α4β7 in pathogenesis and transmission.

MD3.6

Evidence for HIV-1 subtype-specific constraints on viral escape from host cellular immunity

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Background: HIV-1 adapts to HLA alleles expressed by infected hosts and host populations. However, the extent to which HIV's genetic context influences population-level adaptation to HLA remains incompletely understood. The Ugandan HIV epidemic, where subtypes A and D co-circulate, provides a unique opportunity to distinguish universal pathways of HIV adaptation from those that are subtype-specific.

Methods: High-resolution HLA class I and HIV RNA *gag* genotyping were performed for 513 antiretroviral-naïve patients from Kampala and Mbarara, Uganda. Recombinant and non-A/D sequences were excluded, leaving 200 subtype A and 135 subtype D *gag* sequences for analysis. HLA-associated polymorphisms were identified in each subtype via statistical association with phylogenetic correction, after which a logistic regression approach was used to determine cases where the same HLA allele drove significantly different escape pathways between subtypes.

Results: Of 103 unique HLA alleles observed in the study cohort, only 3 (B*58:01, C*16:02, A*26:12) differed in frequency between subtypes A and D ($p<0.05$), consistent with a single host population where HIV subtypes co-circulate. A total of 55 HLA-associated polymorphisms at 25 Gag codons were identified at the population level in subtype A; 36 HLA-associated polymorphisms at 25 Gag codons were identified in subtype D ($p<3x10^{-4}$, $q<0.2$). Comparative analysis revealed that >35% of these adaptations differed significantly between subtypes. For example, B*57:03 drove the selection of T242N in subtype D (Odds Ratio~250, $p=2x10^{-10}$) but not in subtype A (inter-subtype comparison $p=8x10^{-6}$), whereas Y79F selection by A*01:01 was six-fold stronger in subtype A (OR~20) versus D ($p=2x10^{-3}$).

Conclusions: HIV's genetic context exerts a substantial influence on its ability to adapt to HLA. Establishing whether this is attributable to differential epitope presentation, mutational constraints or other factors is relevant to vaccine design.

Multi-Disciplinary: Community-based HIV Research

Multidisciplinaire : La recherche communautaire sur le VIH

MD4.1

Use of the Vidaview Life Story Board as a novel qualitative interview tool for community-based research among people who use drugs

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Understanding the social contexts and life experiences that surround harm reduction practices is fundamental to the development of effective services and supports for people who use injection drugs (PWID). However, barriers such as memory, low literacy, and negative impressions or experiences of research can render qualitative interviews difficult with PWID. The Vidaview Life Story Board (LSB) is a visual interview tool that uses a magnetized board, sets of cards, markers, and a flexible notation system to construct a visual representation of a person's life circumstances, including personal, family, and community experiences. The LSB facilitates a conversation between "storyteller" or interviewee, the storyboarder who records details on the board, and the interviewer, in a process of co-construction to translate aspects of the narrative into a visual "life-scape". One of the objectives of this study is to pilot test the feasibility, utility, and accessibility of a new qualitative interview tool in a community-based participatory research setting with PWID. Using peer-based street recruitment, we conducted two dozen peer-led semi-structured interviews with PWID using the LSB. Four people with lived experience were trained using the LSB; in pairs, one conducted the interview questions while another documented the participant's harm reduction experiences using the board. In order to enhance our evaluation process, project staff subsequently conducted semi-structured interviews with participants to understand their experience of being interviewed using the board. In addition, a research assistant conducted individual, semi-structured interviews with each peer researcher about their experience conducting LSB interviews with PWID. All interviews were audio recorded, transcribed, and analyzed using content analysis. We will present an evaluation of the LSB as a tool for conducting qualitative interviews with PWID that we anticipate will be applicable to other disadvantaged populations.

MD4.2

The Spectrum of ARVs - What are Women Taking and How Well are they Doing? Findings from the Canadian HIV Women´s Sexual and Reproductive Health Cohort Study (CHIWOS)

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Objectives: To determine the proportion of Canadian women living with HIV who are on antiretroviral therapy (ART), the specific antiretrovirals used and to characterize those who are not virally-suppressed.

Methods: Cross-sectional data was analysed from CHIWOS, a study of 1,425 women with HIV from British Columbia, Ontario and Quebec. The primary outcome was self-reported use of ART; women with missing information were excluded (n=41). The probabilities of ART and agents were summarized using proportions. Multivariable logistic regression was used to identify correlates of being on ART with a detectable viral load (VL) (>50 copies/mL).

Results: Of the 1,384 women, 1,178 (85.1%) were on ART (median= 8.6 years [IQR=4.3-14.7 years]). A single-tablet-regimen was prescribed to 25.7%; 13.9% on Atripla, 8.2% on Complera and 3.6% on Stribild. All but 5% of women were on a NRTI backbone [Truvada (56.4%) and Kivexa (23.2%)]. The most commonly prescribed third agent was an NNRTI (33.2%); boosted protease inhibitors (PIs) (28.8%) and integrase inhibitors (IIs) (15.7%) were also common. Atazanavir was prescribed twice as frequently (14.4%) as darunavir (7.6%); raltegravir was the most common II (10.8%).

Of women on ART with self-reported VL data, 9.0% had a detectable VL with a median CD4 count of 279 cells/mm^3. In multivariable analysis, the odds of being on ART with an undetectable VL were significantly lower among women <30 (aOR=0.49;95%CI=0.25-

0.97;p=0.041), with a history of incarceration (aOR=0.58 for ever;95%CI=0.35-0.97; aOR=0.26 for within last year;95%CI=0.13-0.54;p=0.001) or among non-home-owners (aOR=0.23;95%CI=0.06-0.97;p=0.045 vs. home-owners) and higher for women with higher education (aOR=1.49 for secondary;95%CI=0.87-2.56; aOR=2.50 for post-secondary;95%CI=1.31-4.78;p=0.021) or a higher resiliency score (aOR=1.04;95%CI=1.02-1.07;p=0.002).

Conclusions: We identified the proportion of women with HIV who are on ART (85.1%), virally-suppressed (91.0%), and antiretrovirals used in a large Canadian cohort. Women <30 or those with either a history of incarceration or lower education should receive particular attention.

MD4.3

"Who is there to support our women?": Positive Aboriginal Women (PAW) speak out about health care experiences and needs during pregnancyand birth

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Introduction: To date, there remains insufficient research on the pregnancy experiences of Positive Aboriginal Women (PAW) that considers their socio-historical and political contexts while responding to their perinatal care experiences and desires. Drawing on the experiences of 29 PAW from Ontario, Saskatchewan and British Columbia, this paper highlights the clinical care challenges and desires that PAW experience, as well as recommendations for practice with PAW during pregnancy and childbirth.

Methods: Grounded in a community-based research framework, qualitative data was collected using narrative interviews in Ontario and through sharing circles in Saskatchewan and British Columbia. Narrative interviews were conducted with HIV Mothering Study participants in Ontario who identified as First Nations (n=5) in pregnancy and at 3 months postpartum. Sharing circles were conducted with PAW in Regina (n=7), Saskatoon (n=11) and Vancouver (n=6) as part of community engagement efforts to explore how experiences of pregnancy and birth were similar to or different from women in Ontario; all sharing circle participants identified as First Nations. PAW researchers were integral to our research approach assisting with recruitment, data collection and analysis, and in developing recommendations for culturally-based perinatal practices.

Findings: Historical and present day challenges, as well as acts of resilience and cultural connection, emerged as key themes in PAW's experiences of pregnancy and birth. PAW confront systemic discrimination, HIV-related stigma, and an absence of culturally-relevant healthcare services that result in barriers to HIV testing and exclusionary perinatal care experiences. Resiliency was reflected in PAW's acts of educating one's self about pregnancy in the context of HIV, self-advocacy, and seeking out cultural and peer support.

Conclusion: Addressing the perinatal care needs of PAW requires increased attention to addressing barriers to HIV testing and clinical care, and in advocating for culturally responsive resources. PAW leadership is imperative to the success of this response.

MD4.4

Mapping Home: Using Maps of Living Spaces to Augment Interview Data on HIV and Housing

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Background: Positive Living, Positive Homes is a community-based research study examining the complex relationship between health and housing for people living with HIV in British Columbia. In-depth interviews include a mapping component, in which participants from a wide range of housing situations are asked to draw their current home. The aim of this analysis is to explore the usefulness of the maps in augmenting the interview information.

Methods: To date, 82 people living with HIV have participated in interviews in three BC communities. In order to ensure comfort of participants with diverse drawing/literacy skills, we provided drawing tools and framed the activity in a non-threatening way (i.e., mapping facilitates understanding of the relationship between wellbeing and space, and does *not* need to be a perfect representation of the space). We purposively selected (based on community, personal characteristics, and map diversity) hand-drawn, colour-coded maps from 35 participants. Maps were analyzed using a participatory approach consistent with CBR and GIPA/MIPA principles.

Results: Some aspects of the home increased feelings of wellbeing (windows, plants, relaxing spaces), while others decreased wellbeing (pests, lack of privacy, space constraints). In addition to physical aspects, social relationships were linked to health, indicating that these are important elements of "home" to consider. Despite visual/structural similarities, participants interpreted questions and generated maps differently, revealing that identity markers such as gender and cultural background, as well as preferences and expectations, influence how participants construct a sense of home. Although the visual mapping augmented study findings, it was essential to match maps with interview transcripts to allow for thorough interpretation.

Conclusions: Visual research methods offer alternate ways of understanding and articulating connections between health and place. When carefully planned as part of the

interview process, mapping can deepen understanding of how housing and health interact for people living with HIV.

MD4.5

Exploring harm reduction practices among people who use injection drugs through use of qualitative interviews with the Vidaview Life Story Board

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Prevention and treatment programming must be informed by understanding the social contexts and life experiences that surround harm reduction practices. This qualitative study was conducted in Ottawa, Canada, where, among the almost 6,000 people who use injection drugs (PWID), HIV and hepatitis C rates are high at approximately 15% and 60% respectively. Injection practices considered high-risk for HIV and hepatitis C transmission remain common. As such, one of the objectives of this study was to improve our understanding of the use of harm reduction strategies among PWID, a goal identified as a priority by our local Community Advisory Committee. However, barriers of literacy, memory recall, and negative past experiences or perceptions of research can diminish the utility of traditional qualitative interviews among PWID. Using peer-based recruitment, we conducted 24 interviews with PWID using the Vidaview Life Story Board, an innovative interview tool where interviewers and participant co-construct a visual "life-scape" using a board, cards, markers, and customized picture magnets. In pairs, peer researchers facilitated the interviews: one administered the interview questions while the other documented the participant's story using the board. Interviews explored harm reduction histories, facilitators and barriers to harm reduction practices, and suggestions for improving services and supports. Interviews were audio recorded, transcribed, and analyzed using interpretive phenomenological analysis. Results include descriptions of the harm reduction practices and services that PWID use as well as how they use them, their motivations for using harm reduction, and changes in their use of harm reduction over time. These findings demonstrate the key influence of social support on harm reduction, the need for increased access to harm reduction services among high risk groups, and the importance of addressing this issue from a social justice standpoint.

MD4.6

"My focus is getting out into society." Exploring activity and social participation needs and goals of people living with HIV

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Background: Health and social care systems are challenged to respond to the evolving needs and goals for ongoing engagement in valued activities by people living long-term with HIV.

Purpose: Through this community-based qualitative study we explored how people living with HIV endeavoured to engage in valued activities. In particular, we sought greater understanding about what types of supports people needed to overcome obstacles in their quest to participate in those activities.

Methods: We recruited 19 people with diversity in age, sex, and experience of disability from a community health centre and a hospital-based HIV program. We conducted two focus groups and four individual interviews. Interviews were audio-taped and transcribed verbatim. Data were analyzed using inductive qualitative methods.

Results: Participants' valued activities ranged from exercising and socializing to parenting, volunteering and working. Many strove to engage in activities to reap diverse benefits that included: counteracting profound boredom, improving physical and mental health, planning for an uncertain future, and contributing to society. In addition to the symptoms of their health conditions, participants identified five categories of obstacles to engaging in valued activities: 1) fear and worry, 2) stigma and discrimination, 3) unmet basic needs, 4) limited resources, and 5) inadequate supports and services. Participants provided perspectives on their needs for trusted professional and peer supports and services to help them 1) explore the possibilities, 2) gain skills and experience, and 3) access resources and opportunities to engage in valued activities.

Conclusion: Current supports and services do not fully address the unmet needs of people living long-term with HIV who face obstacles when attempting to engage in valued activities. In addition to symptom management, there needs to be greater availability and access to supports that focus on helping people living with HIV to achieve their activity and social participation goals.

Basic Sciences: Virology

Sciences fondamentales : Virologie

BS3.1

In Vivo Control of HIV Infection via Gene Therapy with a Secreted Entry Inhibitor

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HIV entry inhibitors are highly effective in controlling HIV replication, but their clinical use is limited due to the need for frequent injections of highly purified proteins and the associated costs. Modifying patient cells to constitutively secrete entry inhibitors may alleviate the need for continuous drug administration and serve as an alternative to antiretroviral drug therapy. We have designed a lentiviral vector capable of secreting an entry inhibitor, soluble CD4 (sCD4), which binds to the HIV envelope proteins and inactivates virus particles. Modeling of this approach using humanized mice capable of recapitulating key aspects of the human immune system is critical to the development and implementation of this strategy. Therefore, human $CD34^+$ hematopoietic stem progenitor cells (HSPCs) were transduced with sCD4-expressing or control lentiviral particles. Transduction of HSPCs resulted in high levels of gene marking (25-30%) and expression of sCD4 (1 µg/ml). To investigate the *in vivo* potential of our approach, gene-modified and unmodified HSPCs were injected into NOD/SCID/γc^{null} (NSG) mice. NSG hosts were capable of supporting multi-lineage differentiation from human gene-modified and unmodified $CD34^+$ HSPCs. No major differences between lineage reconstitution by gene-modified and unmodified cells were evident. Upon challenge with HIV, humanized mice capable of secreting sCD4 demonstrated a clear reduction of HIV viral load over time compared to control humanized mice as well as higher levels of CD4+ T cells in the peripheral blood and tissues. Our work provides support for the continuous delivery of secreted entry inhibitors via gene therapy as a therapeutic alternative to antiretroviral drug therapy. We will further investigate the potential of covalently linked bi-functional fusion proteins that target multiple steps of HIV entry.

BS3.2

Leveraging Human Genetic Diversity to Define the Role of Siglec-1 in HIV Infection In Natura

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Siglec-1/CD169 is a myeloid-cell surface receptor critical for HIV-1 capture and infection of bystander target cells. Through mining available genetic data from >63,000 individuals, we identified a low frequency (1%) protein-truncating variant (PTV) in the coding region of the SIGLEC1 gene predicted to knock out its expression in vivo. Exome sequence analysis and direct genotyping of 3,733 HIV-1-infected individuals from the Swiss HIV Cohort Study revealed two SIGLEC1 PTV homozygous and 85 heterozygous subjects, allowing the analysis of ex vivo and in vivo consequences of SIGLEC1 loss of function. Cells from these individuals were null or haploinsufficient for Siglec-1 function in HIV-1 capture and trans-infection. However, Siglec-1 protein truncation did not have a measurable impact on HIV-1 acquisition or AIDS outcomes in vivo, a result that contrasts with its known in vitro functional role in HIV-1 trans-infection. This suggests efficient, alternative paths to HIV-1 infection and highlights the usefulness of human loss-of-function variants to dissect biological principles.

BS3.3

Role of Antibody-Dependent Cell-mediated Cytotoxicity in HIV-1 Uninfected Bystander CD4+ T Cell Killing

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HIV-1 infection causes a progressive depletion of CD4+ T cells. Despite its importance for HIV-1 pathogenesis, the precise mechanisms underlying CD4+ T cell depletion remain incompletely understood. We recently reported that gp120–CD4 interaction in infected cells results in exposure of antibody-dependent cell-mediated cytotoxicity (ADCC) epitopes recognized by anti-Env antibodies present in sera from HIV-1-infected individuals. Here we make the surprising observation that ADCC mediates the death of uninfected bystander CD4+ T cells in cultures of HIV-1-infected cells. While HIV-1-infected cells are protected from ADCC

by the action of the viral Vpu and Nef proteins which limit Env-CD4 interaction, uninfected bystander CD4+T cells bind gp120 shed from productively infected cells and are efficiently recognized by ADCC-mediating Abs such as A32 and sera from HIV-1-infected individuals. This is independent of viral coreceptor usage and was observed using a variety of HIV-1 variants including transmitted/founder viruses. Thus, gp120 shedding represents a viral mechanism to divert ADCC responses towards uninfected bystander CD4+ T cells. Importantly, CD4-mimetic molecules redirect ADCC responses from uninfected bystander cells to HIV-1-infected cells; therefore, CD4-mimetic compounds might have therapeutic utility in new strategies aimed at specifically eliminating HIV-1-infected cells.

BS3.4

Combination of RNA molecules targeting the HIV-1 RNA for use in gene and drug therapy

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Background: The only confirmed case of an HIV-1 functional cure is from an individual who received an allogeneic cell transplant from an HIV-1 resistant donor. The closest feasible procedure would be to use autologous transplant with gene modified HIV-1 resistant cells. One approach involves modifying cells to produce a combination of antiviral genes that can control HIV-1 replication over a long period of time. Although several candidate combinations have been proposed, there is limited data available on the comparative efficacy of different molecules and on their effects in combination with one another.

Methods: We have selected several ribozymes derived from the hepatitis delta virus (HDV), small interfering RNAs (siRNAs) and short hairpin RNAs (shRNAs) targeting conserved regions of HIV-1 RNA. We have expressed them on vectors and tested their efficacy on HIV production after transfecting HEK293T cells. The most active were chosen and their sequence length was optimized for efficacy. Assays on cell proliferation and on interferon induction were used to evaluate their toxicity.

Results: We have identified HDV-ribozymes, siRNAs and shRNAs targeting a conserved region of HIV Gag RNA. We evaluated different starting positions and stem lengths for both shRNAs and siRNAs. Our results showed that siRNAs of 27-29 base pairs or shRNAs with 20-21 base pairs have the strongest potency to inhibit HIV production with no potential toxicity. Among several anti-HIV RNAs, the optimal Gag shRNA we identified is one of the two most potent inhibitors of HIV-1 production. Ongoing studies evaluate the efficacy and safety of different combinations.

Conclusion: Our results show that ribozymes, siRNAs and shRNAs targeting HIV Gag RNA are very active to inactivate the virus with no detectable toxicity. These results highlight their potential to be used in combination gene therapy or as drugs to contribute to a cure against HIV-1 infection.

BS3.5

HIV-1 Env but not Nef protein overcomes the inhibition by the ectopically expressed SERINC5

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SERINC5 was recently reported as a potent host restriction factor. HIV-1 Nef protein counters SERINC5 restriction albeit that ectopically expressed SERINC5 still diminishes the infectivity of the wild type HIV-1 strain NL4-3 (Nef positive) by more than 50 fold. In this study, we tested a number of different HIV-1 strains for their susceptibility to the inhibition by ectopically expressed SERINC5 and found that two HIV-1 primary isolates named AD8.1 and YU-2 were resistant. Inserting the Env sequence from AD8.1 into NL4-3 generated a chimeric virus that was as resistant to SERINC5 as AD8.1. Further mutagenesis studies revealed that the V3 loop alone from AD8.1 was able to transform the Nef-defective NL4-3 from a SERINC5-sensitive to a SERINC5-resistant virus. Similar levels of resistance to ectopically expressed SERINC5 were also observed when the glycoprotein G of vesicular stomatitis virus was used to pseudotype virus particles. These data suggest that in addition to the Nef protein, HIV-1 Env provides a strong mechanism to overcome the restriction imposed by high levels of SERINC5.

BS3.6

Plasma MicroRNA profiling predicts HIV-Associated Neurocognitive Disorder

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Background: The development of HIV-associated neurocognitive disorder (HAND) can be influenced by several factors including altered host and viral gene expression. Host-encoded microRNAs (miRNAs) have been shown to contribute to the pathogenesis of HAND and thus serve as biomarkers of diagnosis and prognosis. Herein, we investigated plasma microRNA profiles among HIV/AIDS patients with and without HAND.

Methods: Plasma microRNAs was measured in HAND (n=22) or nonHAND (n=25) patients (Discovery Cohort) by array hybridization (Affymetrix 3.0 miRNA genechip). Two software packages (Affymetrix Expression Console and Gene Spring) were used to normalize data and determine

differentially expressed miRNAs. The median of each probeset in the HAND or nonHAND was calculated after normalization and differentially expressed miRNAs were identified. A second cohort (Validation Cohort) consisting of prospectively recruited HAND (n=12) and nonHAND (n=12) patients was used to validate the miRNA profile in Discovery Cohort.

Results: Expression analyses identified 9 miRNAs in the Discovery Cohort (HAND, n=22; nonHAND, n=25) with increased levels ($\geq$2.0 fold) in the HAND group compared to the nonHAND group ($p<0.05$). In the Validation Cohort (HAND, n=12; nonHAND, n=12) up regulation ($\geq$2.0 fold) of 3 miRNAs was observed in the HAND group that were also increased in the Discovery Cohort's HAND patients, which were verified subsequently by qRT-PCR. Receiver-operating characteristic curve analyses for the 3 microRNAs also pointed to the diagnosis of HAND diagnosis (Area under curve, 0.87, $p<0.005$). Bioinformatics tools predicted that all 3 miRNAs targeted sequences of genes implicated in neural development, cell death, inflammation, cell signalling and cytokine functions.

Conclusions: Our findings revealed differential expression of three cell plasma-derived miRNAs in HAND versus nonHAND patients. These results suggest that plasma miRNAs might be used as biomarkers for HAND and also provide insights into the underlying disease mechanisms.

BS3.7

Latently HIV-1 infected cells have defects in the type I IFN response that can be exploited for killing by oncolytic viruses

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Background: Latent HIV reservoirs represent the major barrier to eradication. The type-I interferon (IFN-I) response is an integral antiviral defense, but is impaired during productive HIV infection. Defective IFN-I signalling in cancer cells has been exploited for the development of therapeutic oncolytic viruses (OV), including the recombinant Vesicular Stomatitis Virus (VSVΔ51) and Maraba virus (MG1). If IFN-I defects are present in the latent reservoir, we hypothesize that OV can selectively kill latently HIV-infected cells.

Methods: Utilizing the latently HIV-infected OM10.1 cells and parental HIV-uninfected HL60 cells, IFN-I signalling was evaluated by measuring IFNAR1, MHC-I, PKR, and ISG15 by flow cytometry, both at basal levels and in response to IFNa. To investigate the ability of OVs to selectively target latently HIV-infected cells, HL60 and OM10.1 cells were infected with GFP-expressing VSVΔ51 or MG1. OV infection was quantified by flow cytometry. PI, MTT, and Alamar Blue assays were used to assess cell viability. Effect of OV infection on HIV expression was evaluated by reactivation of HIV with the HDACi Vorinostat and quantification of total p24-antigen expression.

Results: Basal expression of IFNAR1 and MHC-I, as well as IFNa induced expression of PKR and ISG15 was impaired in latently HIV infected OM10.1 cells compared to HL60 cells. In parallel, OM10.1 cells were significantly more susceptible to VSVΔ51 and MG1 infection and killing than HL60 controls in both a dose- and time-dependent manner. HIV reactivation with Vorinostat significantly enhanced OV-cytopathic effects, with an associated decrease in p24 expression.

Conclusion: The latently HIV-infected OM10.1 cells, in contrast to HIV-uninfected HL60 cells, exhibit significant defects in the antiviral IFN-I response pathway. This impaired IFN-I responsiveness was associated with increased infection and killing by VSVΔ51 and MG1. Therefore, targeting impaired IFN-I signalling may represent a novel and effective approach to selectively target and eliminate the latent HIV reservoir.

BS3.8

A significant role for Nef's N-terminal alpha-helix domain in its ability to sequester Lck and inhibit T cell signalling

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Background: The HIV-1 Nef protein modulates CD4 T cell activation by interacting with host signalling proteins. Nef binds to tyrosine kinase Lck, which promotes proximal T cell receptor (TCR) events, and sequesters it near the trans-golgi network (TGN). We have shown that Nef inhibits NFAT transcription factor activity following TCR stimulation in Jurkat cells. To identify motifs that contribute to this phenotype, we examined a panel of Nef mutants for their ability to inhibit TCR signalling and to relocalize Lck.

Methods: We constructed Nef (SF2 strain)-GFP products with mutations in motifs that affect myristoylation (G2A), N-terminal alpha-helix formation (R4A4), CD4 (LLAA) or HLA class I (M20A) down-regulation, and Pak2- (F191I) or Lck-binding (AXXA). Jurkat cells were co-transfected with each Nef-GFP and an NFAT-driven luciferase plasmid, and GFP+ cells were sorted at 18 hr. NFAT signalling was measured by luminescence after a 6 hr stimulation with anti-CD3 Ab (in triplicate). Co-localization of endogenous Lck with TGN was measured by confocal microscopy in unstimulated cells (avg. 57 cells per mutant).

Results: WT Nef inhibited NFAT signalling and relocalized Lck to TGN, while the G2A variant lacked both activities. The AXXA mutant had reduced ability to inhibit NFAT (71% compared to WT) and, as expected, was unable to relocalize Lck. The R4A4 mutation had an even greater impact on NFAT inhibition (57% of WT) and sequestered Lck at only 31% of WT. Interestingly, F191I was impaired for signalling

inhibition (80% of WT) and Lck sequestration (41% activity). Nef's CD4 and HLA down-regulation activities were not associated with signalling effects.

Conclusion: Our results indicate that Nef's N-terminal alpha helix plays a significant role in its ability to inhibit TCR signalling. Nef motifs involved in modulating T cell activation state may be distinct from those needed for CD4 and HLA downregulation functions.

Clinical Sciences: HIV and Comorbidities

Sciences cliniques : VIH et comorbidités

CS3.1

Mitigating the impact of selection bias on estimates of HAND prevalence

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Background: Estimates of the prevalence of HIV-Associated Neurocognitive Disorders (HAND) have been derived from rates of impairment on neuropsychological testing. The extent to which individuals tested are representative of the population of individuals living with HIV has rarely been documented. The aim of this study is to test the extent to which HIV+ individuals who accepted vs refused participation in a cohort study on brain health differed on baseline indicators.

Methods: The Positive Brain Health Now study invited all eligible patients followed at one Montreal clinic to participate. Selection criteria: age ≥ 35, HIV+ ≥ 1 y, absence of dementia or neurological disorders. All persons approached were asked to complete a questionnaire to estimate the potential for selection bias. Age, sex, working status (y/n), reason for refusal, and two questions on cognitive difficulties were compared between acceptors and refusers. Logistic regression was used to test whether the predictors of work status differed between the two groups. Regression parameters were converted to odds ratios (OR) with 95% confidence intervals (95%CI).

Results: 410 eligible patients were approached: 261 refused, with 182 of those completing the refusers questionnaire. Refusers were more likely to be <45 y/o, women, less likely to report cognitive difficulties, and almost twice as likely to be working as acceptors (OR: 1.92; 95% CI: 1.4-3.24).

Conclusions: There was a high rate of refusal to enter the study, raising serious concerns about bias, which would limit the generalizability of the results and likely inflate HAND prevalence estimates. Collecting key data on refusers showed that the relationship of reported cognitive difficulties, age, and sex to working was the same for refusers and participants. These findings will permit estimates derived from the participants to be generalized to refusers. The results reinforce the need to systematically document key variables for those refusing study entry.

CS3.2

Brain Dysfunction in HIV: Clustering of Cognitive and Motivational/Affective Symptoms

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Background: Untangling the different "phenotypes" of brain dysfunction in HIV will allow more focus in studying the causes and testing treatments. The objective of the present study was to estimate the extent to which cognitive, motivational, affective symptoms and fatigue cluster among people with HIV.

Methods: The data came from the Positive Brain Health Now study, a Canadian cohort of people with HIV (≥ 35 years). Cognition was assessed using the Perceived Deficits Questionnaire and computerized cognitive tests (B-CAM); mood and anxiety were measured using the HADS, motivation was measured using a shortened version of Starkstein's Apathy Scale, and fatigue was measured using the Vitality subscale of the RAND-36. All values were calibrated on a 0 to 100 scale with 100 indicating the absence of symptoms. A principle component analysis was carried out to create a single cognitive factor. The five symptom constructs were transformed into age-and education-standardized values and subjected to a cluster analysis.

Results: A total of 738 observations were available and 30 clusters best fit the structure of the data. To better visualize the clustering, the mean standardized scores were transformed to ordinal values as follows: good, >+0.5; neutral, -0.5 - +0.5; poor: <-0.5- -2.0; and lowest: <2.0. Six superclusters emerged and were summarized in 4 phenotypes. The largest phenotype represented people who were good or neutral on all constructs. Very few participants (n=6) performed poorly on all constructs. Among people already showing evidence of brain dysfunction, two phenotypes predominated: (i) anxiety/depression with or without cognitive difficulties; and (ii) low motivation, with or without problems with cognition and/or fatigue.

Conclusions: Our next step is to identify the HIV and clinical factors discriminating between these phenotypes and to identify whether there is a differential effect of phenotype on lifestyle, physical function, social role, work, or quality of life.

CS3.3

Prevalence and Cofactors of Nonalcoholic Fatty Liver Disease diagnosed by Transient Elastography with Controlled Attenuation Parameter in HIV Mono-infection

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Background: Nonalcoholic fatty liver disease (NAFLD) is the most frequent liver disease in Canada. HIV+ persons are at high risk for NAFLD. Nevertheless, data on NAFLD in HIV mono-infection are scarce.

Methods: We investigated prevalence and cofactors of NAFLD and liver fibrosis by transient elastography (TE) and associated controlled attenuation parameter (CAP). This was a prospective cohort study of HIV mono-infected adults without significant alcohol intake or coinfection with hepatitis B or C. Any grade NAFLD (involving >10% of hepatocytes), significant NAFLD (>30%) and severe NAFLD (>60%) were defined as CAP>232, CAP>260 and CAP>292dB/m, respectively. Significant liver fibrosis and cirrhosis were defined as TE measurement >8 and >13 kPa, respectively. Cofactors of NAFLD and liver fibrosis were determined using logistic regression.

Results: 310 consecutive patients (mean age 49.9 years, 77% men; mean CD4 630±253, 90% on antiretrovirals) were included. CAP identified any grade, significant and severe NAFLD in 55.3%, 33.7% and 16.3% of cases, respectively. Significant liver fibrosis and cirrhosis were found in 11% and 2.3% of cases, respectively. Multivariate analysis results are reported in the Table. The presence of at least two predictors among BMI>25, exposure to protease inhibitors and elevated ALT had 100% sensitivity to rule in significant NAFLD.

Conclusion: NAFLD diagnosed by TE with CAP is frequent in HIV mono-infected persons, particularly in those with obesity, elevated ALT and exposed to protease inhibitors. Importantly, significant NAFLD was an independent predictor of liver fibrosis. Non-invasive screening strategies should be implemented for such a frequent comorbidity in this population.

	Significant NAFLD (CAP>260dB/m)	
Variable	**Adjusted OR (95% CI)**	**p**
BMI>25 Kg/m^2	4.44 (2.26-8.72)	<0.001
ALT>Upper Limit Normal	2.35 (1.14-4.84)	0.02
Exposure to protease inhibitors	2.43 (1.19-5.00)	0.02
	Significant Liver Fibrosis (TE>8kPa)	
Variable	Adjusted OR (95% CI)	p
Age	1.11 (1.04-1.18)	0.002
BMI>25 Kg/m^2	2.91 (1.02-10.29)	0.04
ALT>Upper Limit Normal	8.30 (2.45-28.06)	0.001
Significant NAFLD		
(CAP>260 dB/m)	5.82 (1.68-20.11)	0.005

CS3.4

Association between HIV-related factors and white matter hyperintensities (WMH) on brain MRI among HIV+ adults treated with HAART

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Background: WMH occur in a normal, aging population and are associated with increased risk of stroke, cognitive decline, dementia, and death. It is unknown whether WMH are a feature of neurocognitive impairment among HIV-infected adults.

Objective: To evaluate whether HIV/HAART-related factors are associated with the burden of WMH.

Methods: HIV+ adults with any degree of self-reported impairment in cognition, memory and concentration not explained by another diagnosis were referred for comprehensive evaluation and recruited for this cross-sectional, cohort study. In a subset, head MRI was indicated to rule out structural lesions, opportunistic infections and other confounding conditions. Each MRI was scored using 2 standardized WMH visual rating scales. Both are modified numerical scores based on the severity of WMH scored from 0-3 in 8 locations (Fazekas score) or 4 locations (Age-related white matter changes [ARWMC] score) in the brain. HIV/HAART-related factors were derived from the provincial HIV Drug Treatment Program.

Results: 81 adults were included in the main cohort and 60 had MRI results (Table 1). There was a strong positive correlation between the WMH scores ($r = 0.843$, $p < 0.001$), but no significant correlation of either score with age, gender, history of AIDS-defining illnesses, hepatitis B/C co-infection, current or nadir CD4+ count, baseline and current plasma viral load, duration of HIV diagnosis, or time on HAART.

Conclusions: The majority of the study population had a burden of WMH on MRI that would not be considered clinically significant for their age. WMH were not associated with any HIV/HAART-related factors.

Table 1: Characteristics of study population (N=60)

Category	Value	Interquartile Range
Median age, years	53	47, 59
Male gender, N (%)	57 (95.0%)	
Previous AIDS-defining illness, N (%)	32 (53%)	
Median current CD4+, cells/mm3	485	360, 685
Median CD4+ nadir, cells/mm3	150	55, 240
Median time since HIV diagnosis, years	11.2	6.4, 16.7
Median duration on HAART, years	6.1	3.3, 9.5
Ever diagnosed with Hepatitis B, N (%)	2 (3.3%) (7 unknown)	
Ever diagnosed with Hepatitis C, N (%)	14 (23.3%)	
Median Fazekas score	5	4, 8
Median ARWMC score	1	0, 2
Abnormal Fazekas score (>9), N (%)	12 (20.0%)	
Abnormal ARWMC score (>4), N (%)	4 (6.7%)	

CS3.5

The State of Health: The Impact of Select Co-morbidities on Life Expectancy

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Background: Healthy life expectancy (HLE) combines age-specific mortality with morbidity to estimate expected years of life in good health for persons at a given age. We aimed to estimate HLE at 20 years of age for select comorbidities among adults living with and without HIV in British Columbia (BC).

Methods: Our sample included BC residents ≥20 years of age living with and without known HIV from 2000 to 2012. Persons living with HIV (PLHIV) had to have started HAART. HIV- adults were included in a 10% random sample generated from all known HIV- adults in BC. Prevalence of select comorbidities (see Table 1) was calculated using case-finding algorithms. HLE was defined as the absence of these co-morbidities, taking into account background mortality patterns and healthy state as the proportion of life expectancy comorbid free.

Results: For PLHIV, HLE ranged for selected conditions from 32 to 37 years among men and 19 to 32 years for women (see Table 1). Variations in the length of the healthy state for PLHIV and HIV- adults, respectively, included: liver diseases (Men: 65 vs. 96%; Women: 52 vs. 97%), Hepatitis B (Men: 82 vs. 99%; Women: 69 vs. 99%), and renal diseases (Men: 79 vs. 94%; Women: 41 vs. 95%).

Conclusions: HLE varied considerably among PLHIV, especially among women. Notable differences in healthy state length were observed by HIV-status for liver and renal diseases and Hepatitis B. However, for all co-morbidities, HLE was lower for PLHIV.

Table 1 Health life expectancy at age 20 years among British Columbians over the period 2000 to 2012, by select group and sex.

Condition	Group	HLE	Healthy state	HLE	Healthy State
		Males		Females	
Cardiovascular	PLHIV	33.2	81.0%	31.6	90.0%
	HIV-	43.9	78.1%	48.8	81.0%
Repiratory	PLHIV	34.8	85.0%	28.6	81.0%
	HIV-	49.5	88.0%	52.2	87.0%
Liver	PLHIV	26.9	65.8%	18.6	52.9%
	HIV-	54.0	96.0%	58.1	96.7%
Diabetes	PLHIV	35.0	85.9%	31.5	89.7%
	HIV-	47.3	84.1%	51.7	86.1%
Renal	PLHIV	32.1	78.6%	25.0	40.7%
	HIV-	52.7	93.7%	56.8	94.6%
Cancers	PLHIV	34.7	85.1%	32.5	92.4%
	HIV-	51.2	91.0%	55.5	92.4%
Hepatitis B	PLHIV	33.6	82.4%	24.1	68.7%
	HIV-	55.9	99.4%	59.8	99.5%
Hepatitis C	PLHIV	37.1	90.1%	28.5	81.1%
	HIV-	56.1	99.6%	59.9	99.8%

CS3.6

Mitochondrial DNA Content in HIV-unexposed uninfected (HUU) and HIV-Exposed Uninfected (HEU) Children with Autism Spectrum Disorder

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Background: A high prevalence of **autism spectrum disorder (ASD)** in HEU children noted by Canadian pediatricians prompted our analysis of children enrolled in the pan-Canadian Children & Women AntiRetrovirals & Markers of Aging (CARMA) cohort study. Evidence of mitochondrial DNA (mtDNA) alterations and mitochondrial dysfunction has been reported in **HIV-exposed uninfected (HEU)** and ASD children. We measured and compared leukocyte mtDNA content, in matched groups of HEU and **HIV-unexposed uninfected (HUU)** children with and without ASD.

Methods: CARMA HEU children with ASD were matched 1:3 on age, sex, and, when possible, ethnicity, to HEU children without ASD, HUU controls without ASD, and HUU children with ASD participating in the BC Autism Spectrum Interdisciplinary Research (ASPIRE) program. Available HUU siblings of ASD children were also studied. MtDNA content was assessed using qPCR. Between-group analyses were done using Mann-Whitney U or Student's t-tests.

Results: Among 296 HEU in CARMA, 14 (4.7%) were diagnosed with ASD. HEU children with ASD had the highest mtDNA content of all groups (Table 1).

Conclusions: ASD prevalence in our cohort is substantially above North American prevalence estimates (1.5%). Our results suggest a possible cumulative association between elevated leukocyte mtDNA and both HEU and ASD status, which may contribute to the high ASD prevalence in our cohort. It is unclear if this effect is modulated by exposure to cART or maternal HIV but it is consistent with previous studies suggesting increased mtDNA as a compensating mechanism for mitochondrial dysfunction.

Group	HEU with ASD	HEU	HUU with ASD	HUU
N	14	42	42	49
MtDNA Content median [IQR]	163 [150-179]	115 [91-153]	110 [99-132]	100 [73-121]
P-value				
Vs. HEU with ASD[1]	-	0.020	0.0001	<0.0001
Vs. HEU[2]	-	-	0.210	0.004
Vs. HUU controls[2]	-	-	0.034	-
1 Mann-Whitney U Test 2 Student's t-test				

CS3.7

Impact of syndemics of substance use and depression on annual HIV care engagement and treatment outcomes: Results from the OHTN Cohort Study (OCS)

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Background: Syndemics are important in understanding risk factors for HIV transmission, but far less is known about their effect on HIV care outcomes. We examined the association between syndemics of substance use and depression on HIV care engagement and treatment outcomes.

Methods: Data from 4,058 OCS participants (13,062 person-years follow-up) were used to examine whether the number of syndemic factors (SFs): [recreational drug use; harmful alcohol use; cigarette smoking; and depression] was associated with annual HIV care engagement indicators: [continuous care (CC), on antiretroviral treatment (ART), and suppressed viral load (sVL, < 200 copies/mL)]. Poisson regression models and generalized estimating equations were used to estimate adjusted ratio of proportions (aROP) and 95% confidence intervals (CI).

Results: Reporting more SFs was negatively associated (p<0.0001) with being in CC (no SF: 94.3%; 1 SF: 92.9%; 2 SFs: 90.1%; and ≥3 SFs: 89.2%) and being on ART (no SF: 93.4%; 1 SF: 92.6%; 2 SFs: 90.6%; and ≥3 SFs: 83.9). Among those on ART (n=3,743), reporting more SFs was associated with decreasing levels of sVL (no SF: 96%; 1 SF: 95.7%; 2 SFs: 92.4%; and ≥3 SFs: 86.6%, p<0.0001).

In multivariabe analyses, individuals with two SFs were less likely (aROP: 0.97; 95% CI: 0.95-0.98) to be in CC while people with ≥3 SFs were less likely to be in CC (aROP: 0.96; 95% CI: 0.94-0.98) and to be on ART (aROP: 0.94; 95% CI: 0.91-0.96) compared to those with no SFs. Suppressed viral load also declined with increasing number of SFs (aROP: 0.98; 95% CI: 0.96-0.99 for 2 SFs; aROP: 0.93; 95% CI: 0.91-0.96 for ≥3 SFs).

Conclusion: Syndemics factors can have additive (negative) effects on HIV care engagement and treatment outcomes. Integrating addiction and mental health interven-

tions into HIV care may help to support people living with HIV achieve optimal treatment outcomes.

CS3.8

What Happens in Childhood Matters for Life: Childhood Adversities and Poor Health Outcomes among Participants of the Ontario Cohort Study (OCS)

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Rationale: History of childhood trauma predicts poorer health in adulthood. We explored this by measuring childhood adversities (CA), a construct including both violent and non-violent traumatic experiences, and mental and physical health outcomes in people with HIV.

Methods: Data were collected at 3 OCS sites in Toronto. We assessed CAs using the 7-item National Population Health Survey stress scale. Depression was assessed by CES-Depression scale. SF-36 measured physical and mental health-related quality of life (QOL). Linear regression was used to examine the association between number of CAs and health outcomes.

Results: Sample included 1409 HIV+ adults (20% female, 64% GLBT, and 46% non-white). The median number of CAs was 1(IQR: 0 to 3). 71% reported ≥1 CA and 7% ≥5. Mean CES-D score for the sample was 12.8(SD=12.4). Mean physical and mental QOL scores were 49.4(SD=8.4) and 47.3(SD=12.4), respectively. In unadjusted regression analysis, higher number of CAs was associated with higher levels of depressive symptoms and lower physical and mental QOL (all p-values <0.001). In multivariable regression analysis, those with multiple CAs had significantly higher depressive symptoms (β= 1.99 for 3 CAs; β= 2.98 for 4 CAs; β =3.24 for ≥5 CAs; p-values <0.05) compared to those with no CAs. Mental QOL significantly decreased with increasing number of CAs (β= -3.18 for 3 CAs; β= -2.58 for 4 CAs; and β=-3.10 for ≥5 CAs; p-values <0.01). Participants with ≥5 CAs had lower physical QOL (β= -3.74, p<0.001) than those with no CAs. Models were adjusted for demographics, substance use, HIV disease, and psychosocial variables.

Conclusions: Childhood adversity in our sample is prevalent and strongly associated with poorer health outcomes. Further work is required to understand the role of psychosocial and/or physiologic factors that meditate this association, and to design clinical interventions that address the impact of childhood trauma in HIV.

Epidemiology and Public Health: Epidemiology of HIV and Co-infections

Épidémiologie et santé publique : Épidémiologie du VIH et des coinfections

EPH3.1

Incidence of end-stage liver disease and liver-related mortality in HCV mono-infected vs. HIV/HCV co-infected patients in British Columbia

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HIV/HCV co-infection has been associated with rapid progression to end-stage liver disease (ESLD). We compared incidence rates of end-stage liver disease in HCV mono-infected vs. HIV/HCV co-infected patients during the ART era in British Columbia.

Retrospective population data from the Comparative Outcomes and Service Utilization Trends (COAST) study was used to define cohorts of HCV mono-infection on the basis of International Classification of Disease 9/10 codes, and HIV/HCV co-infection. Incidence of ESLD and liver-related mortality was calculated from 04/1996 to 12/2012, using physician billing and hospital-based administrative data. Individuals with prevalent ESLD at time of cohort entry were excluded. Time to development of ESLD disease was calculated for mono-infected patients vs. co-infected patients using Kaplan-Meier methods. Cox Models were used to examine time to ESLD adjusted for age, gender and IDU status.

Overall 13,499 HIV+ individuals were identified, 20% female, 42% IDU, 31% co-infected with HCV and 74% had ever accessed ART. The baseline median age was 38 years (Q1-Q3 31 – 45). A cohort of 9,932 HCV mono-infected individuals, 38% female, 49% IDU with median age 49 years (Q1-Q3 41 – 56)was identified. The incidence of ESLD was 13.30/1000 person-years (PY) for co-infected individuals and 14.69/1000 PY in mono-infected patients (p=0.092). Rates of liver-related mortality were 1.32/1000 PY vs. 2.36/1000 PY in mono-infected individuals (p < 0.01). For co-infected patients, the probability of ESLD was 6%, 14%, 18% at 5, 10 and 15 years, respectively; and for mono-infected patients, probability of ESLD was 7%, 14%, 16% at 5, 10 and 15 years, respectively. In a Cox model adjusted for age, gender and IDU status, mono-infected individuals had similar risk of ESLD (Hazard Ratio 0.99; 95% CI 0.87-1.12).

In an dministrative dataset HCV mono-infected individuals had similar rates of ESLD but higher liver-related mortality than co-infected individuals.

EPH3.2

The British Columbia Hepatitis Testers Cohort

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The British Columbia (BC) Hepatitis Testers Cohort (BC-HTC) was established to assess and monitor hepatitis C (HCV) epidemiology, burden, and treatment effectiveness in BC, Canada. We describe the development of this enhanced surveillance platform in terms of the cohort construction, data linkage processes, linkage yields and characteristics of linked and unlinked individuals. The BC-HTC includes all individuals tested for HCV and/or HIV or reported as a case of HCV, hepatitis B (HBV), HIV or active tuberculosis (TB) in BC and linked with multiple provincial data holdings: cancer registry; mortality data; medical services plan client roster and medical visits; hospitalizations; and drug dispensations using unique personal health number. The cohort includes data since the inception of each database, generally 20 years of data, until 2012/2013 with plans for annual updates. We computed linkage rates by year and compared the characteristics of linked and unlinked individuals. Of 2,656,323 unique individuals available in the laboratory and surveillance data, 1,427,917 (54%) were included in the final linked cohort, including about 1.15 million tested for HCV and about 1.02 million tested for HIV. The linkage rate was 86% for HCV tests, 89% for HCV cases, 95% for active TB cases, 48% for HIV tests and 36% for HIV cases. In 1992, linkage rates were 40% for HCV negatives and 70% for HCV positives, improving over time to 90% after 2005. The lowest linkage rates were in males, younger testers, and those with unknown residence. The highest linkage rates were in HCV testers (vs. HIV), cases (vs. negative testers), older individuals, and females. Linkage rates for HCV testers with another infection (HIV, HBV or TB) were very high (90-100%). Data from the cohort is providing essential information supporting the development of prevention, care and treatment initiatives for those infected with HCV.

EPH3.3

Update on HIV Strains and Transmitted Drug Resistance in Canada

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Background: The Canadian HIV Strain and Drug Resistance Surveillance Program monitors HIV strains and transmitted drug resistance (TDR) among antiretroviral treatment-naïve persons newly diagnosed with HIV. This update describes HIV strains and TDR among HIV diagnoses from five provinces in 2013.

Methods: HIV genotyping was conducted on diagnostic specimens from persons testing HIV-positive in 2013 in British Columbia, Alberta, Manitoba, Ontario or Nova Scotia. Epidemiologic data collected from HIV case reports were linked to genotype results. TDR mutations were identified using the Stanford HIV Database Calibrated Population Resistance Tool. Distribution of HIV strains and prevalence of TDR were examined by sex, age, race/ethnicity, and reported HIV exposure category.

Results: Of 966 specimens submitted, 841 were successfully genotyped. Distribution of HIV strains was as follows: B (81.0%), C (9.9%), CRF02_AG (3.2%), A (1.4%), others (4.5%). Prevalence of non-B strains was higher among females (45.3% vs 13.5% among males, $p<0.0001$). Overall, 12.6% had any TDR. By drug class, 6.9%, 5.2%, and 2.3% were resistant to NNRTI, NRTI, and PI, respectively; 1.8% had resistance to ≥2 drug classes. TDR was greater among MSM (17.3%) and people who inject drugs (PWID; 11.6%) compared to other groups combined (5.6%, $p<0.001$). TDR was similar among MSM by race/ethnicity: 18.2% among White or Aboriginal MSM; 17.4% to 11.1% among other MSM. Among PWID (n=57), TDR was greater among White (19.4%) compared to Aboriginal persons (5.3%).

Conclusion: HIV drug resistance among treatment-naïve persons potentially indicates onward HIV transmission from persons who have initiated care. While regional interpretation is essential to inform local HIV programs and treatment policy, this analysis provides baseline measures for further examination of TDR and circulating HIV strains among sub-populations. Particular differences in the distribution of TDR by HIV exposure category and race/ethnicity support the need for population-specific HIV prevention and control interventions.

EPH3.4

Rise in early stage diagnosis among key populations with expanded HIV testing in Vancouver, BC

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Background: The STOP HIV/AIDS pilot program was launched in March 2010 with the goal of improving early diagnosis and HIV treatment to reduce transmission. Here we describe a rise in early stage diagnosis in the context of expanded targeted and routine HIV testing strategies.

Methods: HIV testing and diagnosis data were collected from laboratory sources and authorized linkages between public health and clinical databases. Indicators from the STOP expansion period (July 1, 2013 - June 30, 2015) are compared to the STOP pilot period (July 1, 2010 - June 30, 2013) and a historical period (January 1, 2008-June 30, 2010). Early stage diagnosis is defined as a CD4 count greater than 500 cells/mm^3 or acute stage disease, and late stage diagnosis is defined as a CD4 count less than 200 cells/mm^3. HIV exposure categories are self-reported and include men who have sex with men (MSM), people who inject drugs (PWID) and heterosexual.

Results: Testing volume increased 51% in the STOP expansion period over the average observed during the STOP pilot and 131% more than historically. Early stage diagnosis comprised 52% of new diagnoses during expansion compared with 47% during the pilot (p=0.341) and 44% historically (p=0.003). Late stage diagnosis declined from 21% historically to 17% during expansion (p=0.483). The greatest change in early diagnosis was observed among MSM, with 60% of diagnoses being early compared to 47% historically (p <0.001). No significant change was observed among heterosexuals with 35% diagnosed early.

Conclusion: The expansion of HIV testing strategies coincided with the largest proportion of early stage diagnosis since HIV became reportable. In a highly concentrated epidemic, the greatest effect was observed among MSM, implying that the addition of routine testing may act complementary to expanded targeted testing strategies to better meet the goals of early stage diagnosis.

EPH3.5

Estimated national HIV incidence rates among key sub-populations in Canada, 2014

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Objectives: To estimate HIV incidence rates among key sub-populations to inform the allocation of prevention and care resources.

Methods: Multiple methods (workbook method and statistical modelling) were used to estimate the number of new HIV infections among key sub-populations in Canada in 2014. Indigenous population counts and people from HIV-endemic countries (all ages) were approximated using 2011 National Household survey data. The population of gay, bisexual, and other men who have sex with men (MSM) and people who inject drugs (IDU) (aged 15 years and older) were estimated from available literature and survey data.

Results: The estimated number of new HIV infections in 2014 was 2,570 (1,940-3,200); the corresponding national incidence rates were 7.2 (5.5-9.0) per 100,000 for all ages, and 8.6 (6.5-10.7) per 100,000 for persons aged 15 and older. MSM exposure accounted for the greatest proportion (54.3%) of new infections; the estimated incidence rate was 469 per 100,000. Compared to other men, the rate among MSM was 61 times higher. An estimated 270 (180-360) new infections occurred among IDU, with a corresponding incidence rate of 344 per 100,000; 45 times higher non-IDU. An estimated 278 (200 to 360) new HIV infections occurred among indigenous people. The incidence rate among indigenous people [18.2 (13.1-23.6) per 100,000] was 2.7 times greater than non-indigenous people. An estimated 358 (250 to 470) new infections occurred among people from HIV-endemic countries. The incidence rate for this population was 40.6 (28.4-53.4) per 100,000; 6.4 times higher than the rate of all other populations combined.

Conclusions: These calculations indicate markedly different HIV incidence rates among key sub-populations in Canada, and particularly high among the MSM and IDU populations. Despite some uncertainties, these rate estimates provide important evidence that can inform programs and policy.

EPH3.6

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

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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 1990 to 2014.

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: Of the 233 identified HIV-positive women giving birth in Canada in 2014, 35% of MIP were identified in Ontario, 20% in Québec, 18% in Alberta, 11% in BC, 8% in Saskatchewan, and 8% in Manitoba; 70% had acquired HIV heterosexually, 16% through injection drug use (IDU) and 3% perinatally; 54% of mothers were black and 17% were indigenous. .Among the 98% of mothers who received combination antiretroviral treatment cART before delivery, 1 perinatally infected infant was born to a mother with poor adherence. Among the 5 MIP who did not receive cART, there were no perinatal transmissions. Overall, proportion treated with cART has steadily increased from 86.5% in 2007 to 97.8% in 2014. IDU (5.4%) and aboriginals (2.5%) had slightly higher statistically non-significant rates of non-treatment. Among 3210 MIP identified perinatally in the cART era (1997-2014), the overall VT rate was 2.0% but only 0.7% in MIP receiving cART and 0.1% in women receiving >4 weeks of cART. No infected infants beyond 3 months of birth were identified in 2014.

Conclusions: VT rates of HIV in Canada remain very low. There are still a few women every year who are not optimally treated with incomplete eradication of vertical transmission. Efforts to sustain identification and treatment of pregnant HIV-positive women to enhance their health and that of their infants must continue.

EPH3.7

HIV and other Sexually Transmitted Infections among African, Caribbean, and Black Men in Toronto, Canada

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Background: African, Caribbean, and Black (ACB) men account for 16.5% of new HIV diagnoses among men in Ontario. There is substantial evidence that sexually transmitted infections (STIs) are associated with increased likelihood of HIV infection; however, little is known regarding the prevalence of HIV and STI co-infections among ACB men. Additionally, no known studies have investigated whether HIV/STI disparities exist between ACB MSM and men who only have sex with women (MSW).

Methods: A cross-sectional descriptive epidemiological study was conducted with a sample of ACB men (*N*=487) recruited from Toronto. Surveys were used to collect demographic and behavioral data. Biological specimens were collected to screen for HIV and other STIs. Chi-Square was used to compare the prevalence of (1) HIV and current STIs between MSM and MSW and (2) current STIs between HIV-positive and non-infected men. Logistic regression assessed past STIs as predictors of HIV infection.

Results: The prevalence of HIV (9.2%), syphilis (7%), hepatitis B (27.9%), and high-risk anal (8.4%) and penile (21.3%) HPV infections was high in the overall sample. The prevalence of HIV, syphilis, hepatitis B and high-risk HPV infections were significantly higher in MSM than MSW. The prevalence of syphilis, hepatitis B, and high-risk HPV (anal and penile) infections were higher in HIV-positive men than non-infected men. There were increased odds of HIV infection for men with histories of syphilis (*OR*=6.48, p<.01), genital warts (*OR*=4.32, p<.01) or genital ulcers (*OR*=21.3, p<.01). Being MSM increased the odds of syphilis history predicting HIV infection.

Conclusions: The HIV/STI prevalence was high among this community-based sample of ACB men. Current and past STIs were associated with HIV infections, with disparities noted in MSM. STI screening and treatment, including increased access to vaccines to prevent infections such as Hepatitis B and HPV, may help reduce risk of HIV in ACB men.

EPH3.8

Characterizing Manitoba's HIV epidemic: A profile of the Manitoba HIV Program clinical cohort

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Background: The Manitoba HIV Program (MHP) provides care and treatment to 1,200 people living with HIV at two sites: Nine Circles Community Health Centre (NCCHC) and an outpatient clinic within the Health Sciences Centre (HSC). Beyond annual statistics from the Public Health Agency of Canada, little is known about the epidemiology of HIV in Manitoba. MHP is thus developing a clinical cohort of individuals in care that will be linked to provincial administrative data. This paper aims to characterize clinical cohort participants to date.

Methods: Enrolment began in October 2013, with extraction of clinical data beginning January 2015. Preliminary descriptive analyses have been conducted, exploring socio-demographics, comorbidity and co-infection prevalence, and HIV-related indicators. Enrolment, data collection, and analyses are ongoing; by the time of presentation, more in-depth analyses will be available on a larger sample.

Results: By January 2016, 649 clients enrolled in the cohort with data collection complete for 391 (60.2%). Of those, 61% receive care at HSC and 39% attend NCCHC. Mean age of participants is 47.3±11.5 years, 68.3% are male, and most self-identify as Caucasian (*n*=172, 44.1%) or Indigenous (*n*=158, 40.5%). Heterosexual contact is the most frequently reported HIV risk exposure (*n*=270, 68.5%). At entry into care, 35.8% (*n*=139) had CD4 counts ≤200cells/μL, while 56.4% (*n*=219) presented with ≤350cells/μL. Hypertension (18.7%) and diabetes (14.6%) are the most prevalent comorbidities, while 10.7% (*n*=42) presented to care with *Pneumocystis* pneumonia and 5.1% (*n*=20) had active tuberculosis infections.

Discussion: Manitoba's HIV epidemic is driven by heterosexual transmission, which is unique within Canada, and late presentation to care is an alarming trend. Similar to other provinces, Indigenous peoples are disproportionately represented in Manitoba's epidemic. As data collection and analyses continue, a clearer picture of Manitoba's HIV epidemic will arise, providing critical information to healthcare providers and policy-makers regarding future programming priorities.

Social Sciences: Programs and Policy Driven Research

Sciences sociales : Recherche axée sur les programmes et politiques

SS3.1

Living Life on ART: Results of the Sepo II Study in Lusaka, Zambia

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Background: Enhanced ART access in Sub-Saharan Africa over the last decade is transforming HIV into a chronic illness with ups and downs. As such, people in hyperendemic countries like Zambia are likely to have new needs related to *living longer with HIV*. Yet the nature of these needs is unknown.

Objective: To explore the experiences of women and men living long-term with HIV on ART in Lusaka, Zambia to inform health policy and practice.

Methods: "Sepo II" is a qualitative longitudinal study involving in-depth, semi-structured interviews 6 months apart with participants from public and private clinics in Lusaka, Zambia. Thirty-five participants were purposively recruited for variability by gender (17 men, 18 women), time on treatment (1-13 years), and SES. An interpretive analysis was conducted using the collaborative "DEPICT" method. The study was guided by the WHO "International Classification of Functioning, Disability and Health", and O'Brien's "Episodic Disability Framework".

Results: Participants framed life on ART as full of hope and optimism but with new challenges as well. The simultaneously positive and negative aspects played out in three themes: (1) impacts on one's body and life, (2) interventions that are available or missing, and (3) stigma in terms of exacerbation and also acceptance.

Conclusion: Sepo II findings point to shortcomings in the current model of HIV care that focuses primarily on initiating and adhering to ART. These health services are necessary but insufficient for meeting the *new needs of people in Zambia living longer as a result of ART*. E.g., HIV policy and programs also need to address counseling for issues beyond VCT and adherence, and rehabilitation to promote

function and quality of life. Overall, findings from the Sepo II Study promote an evolution of the HIV care continuum to embrace a long-term approach to *living well with chronic HIV*.

SS3.2

Women Aging with HIV/AIDS and Housing: Experiences of Refugee Women

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Background: There are a growing number of older women living with HIV. In general, women in Canada experience more adverse health disparities than men. Nonetheless issues of women aging with HIV continue to be marginalized and subordinated within HIV research, policy and programming. This community-based research study aimed to understand the experiences of housing, issues of stigma and discrimination and socially constructed roles of women aging with HIV and the ways these may impact their health and housing.

Methods: For this study, qualitative data were collected through in-depth interviews with 39 women living with HIV, over the age of 40 years. Twenty (51%) of the participants had refugee status at the time of the interview or in the past. Qualitative data were analyzed using thematic analysis. This presentation focuses on the themes generated from the data collected from women who reported having had a refugee status.

Findings: While refugees in Canada face complex issues, including appropriate and affordable housing, refugee women living with HIV/AIDS bear additional concerns of safety and disclosure, due to previously experienced trauma and unique cultural fears of HIV stigmatization. Personal health and age related issues are compounded by several factors including family obligations, uncertainties of the future due to lack of suitable and sustainable housing, separation from family members, barriers in finding employment and in upgrading skills and education.

Recommendations: Service providers must acknowledge and become more aware of issues of disclosure and stigma, and devise culturally appropriate approaches to service provision; build capacity of staff to better support service users with issues of trauma and dislocation through trauma informed training practices; explore options to develop housing suitable for supporting multi-generational or large family units.

SS3.3

The Loss of Boystown and Transition to Online Sex Work: Strategies and Barriers to Increase Safety among Men Sex Workers and Clients of Men

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Background: Men sex workers in Vancouver have largely transitioned from street to online solicitation, coinciding with the loss of "Boystown", the main outdoor sex work stroll for men. This paper aims to explore how the Internet and loss of Boystown have shaped strategies and barriers to increase safety among men sex workers and clients of men in Vancouver, Canada.

Methods: Qualitative interviews were conducted (2012-2013) with 61 cisgender and trans* men who currently buy and/or sell sex from CHAPS (Community Health Assessment of Men Who Purchase and Sell Sex). Drawing on a socio-ecological framework, thematic analysis of interview transcripts was conducted on the loss of Boystown and shift to online, utilizing ATLAS.ti 7 software, among men who buy or sell sex (39 workers; 8 buyers).

Results: Narratives indicate that losing Boystown led to a loss of social support networks among men in the sex industry. Concurrently, significant reorganization of sex work and the shift to online increased workers' safety and control over working conditions. Narratives reveal how soliciting online provides greater opportunities to negotiate the terms of sex work (e.g., prices, types of services, condom use) and enhanced screening of clients using webcams, reducing risks of violence, stigma and police harassment for both workers and clients as compared to street.

Conclusions: Gentrification and urban planning led to social isolation and loss of community and solidarity: key protective measures for sex workers. The shift to online and re-structuring of sex work has increased workers' capacity to screen clients and prevent violence. Recent legal reforms in Canada to further criminalize sex work (i.e., targeting clients, self-advertising), raise significant concern for human rights and health of men in the sex industry, and point to the critical need to include voices of men and trans* sex workers and buyers in policy discussions.

SS3.4

Understanding The Health Status and Healthcare Needs of Gay And Other MSM In The Ottawa Area

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Introduction: A recent analysis showed gay and other men who have sex with men (GMSM) accounted for 77% of incident HIV infections in Ottawa, higher than the prov-

incial average. In view of this, we wanted to determine if GMSM in Ottawa are engaged in healthcare and whether the healthcare they receive addresses their concerns.

Method: A survey of GMSM in Ottawa was conducted enquiring about their health and healthcare needs. The survey was accessible online and in paper format and was promoted through community and professional organizations, the Sexual Health Centre, social media, and online sex websites. Data were compiled and analyzed using SPSS software.

Results: A total of 674 GMSM completed the survey. Overall, GMSM in Ottawa appear to be engaged with the healthcare system: 87% reported having a primary care provider (PCP) and of these 90% reported seeing their PCP at least once annually. However, 24% have not disclosed their sexual orientation to their PCP. A full 31% of GMSM reported a diagnosis of depression and/or anxiety, far above that of the general population. Of concern, 32% reported sadness and 39% reported anxiety interferes with their daily living at least half of the time. In terms of sexual health, 12% reported being HIV-positive, although 8% either were unaware of their status or had never been tested. Two-thirds of men felt only somewhat comfortable or uncomfortable speaking to their PCP about sex, contributing to low levels of awareness of biomedical HIV prevention methods PrEP (53%) and PEP (58%).

Discussion: Although the majority of GMSM in Ottawa have PCPs who they see at least annually, significant gaps exist in the healthcare they receive including HIV risk reduction, and mental, sexual, and anal health. Eliminating these gaps in Canada will require an informed and comprehensive approach to gay men's health.

SS3.5

Ethical Considerations of Providing Online Sexual Health Outreach for Gay, Bisexual, Two-Spirit and Other MSM (GB2M) among Outreach Workers

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Background: GB2M have been early adopters of online technologies. Mobile applications and socio-sexual networking websites are used by outreach workers to synchronously respond to questions and provide information, resources, and referrals on sexual health and STI/HIV prevention, testing, and care. This study sought to identify and address the ethical considerations of online outreach workers who conduct online synchronous sexual health outreach to GB2M. As online sexual health outreach among GB2M demonstrates an important and potentially effective means of providing HIV/STI counseling and intervention, it is critical to understand the ethical implications.

Methods: Thematic analyses were conducted using NVivo10 data analysis software. Inferences from the data were drawn following inductive analysis and grounded in the study's objectives to examine ethical implications of delivering online outreach services for GB2M in Ontario. Semi-structured individual interviews were conducted with online outreach providers and managers ($n = 22$) to explore the benefits, challenges, and implications of delivering online outreach services. Interviews were digitally recorded and transcribed verbatim. Member-checking, analyses by multiple coders, and peer-debriefing supported validity and reliability.

Results: Four themes emerged on ethical queries of providing online sexual health outreach for GB2M: (a) managing personal and professional boundaries with clients; (b) disclosing personal or identifiable information to clients; (c) maintaining client confidentiality and anonymity; and (d) security and data storage measures of online information. Participants illustrated familiarity with potential ethical challenges, and discussed ways in which they seek to mitigate and prevent ethical conflict.

Implications: For *outreach workers*, the results suggest identifying competencies associated with ethical online sexual health outreach. For *managers* in AIDS service organizations, it is critical to understand and mitigate ethical intricacies of online sexual health delivery. For *funders/policy makers* it is important to establish research initiatives that inform evidence-based guidelines to enhance ethical clinical practice and agency standards.

SS3.6

Demographic, Sexual, Testing, and Online Behavioural Differences of Bisexual Men Who Have Sex With Men (MSM) in Ontario

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Background: While online sex-seeking may be associated with HIV risk for MSM, little is specifically known about bisexual-identified men. We examined: 1) demographic, sex, testing, and online behavioural differences between bisexual and other-identified MSM, and 2) condom use during anal sex among bisexual MSM.

Methods: Data were drawn from a community-based anonymous online questionnaire of Ontario MSM. Logistic regression (LR) and chi-square tests were used to assess differences between bisexual-identified MSM and other-identified MSM (e.g., gay, queer). LR was also used to assess associations with condom use during last male anal sex event among bisexual MSM.

Results: Of 1830 MSM, 438 (24.0%) self-identified as bisexual. Bisexual MSM were less likely than non-bisexual-identified MSM to: 1) be HIV-positive (2.4% versus 9.9%; OR=0.23, 95%CI:0.18-0.43), 2) live in Toronto (12.1% versus 34.9%; OR=0.26, 95%CI:0.19-0.35), 3) have a bachelors degree (26.1% versus 43.5%; OR=0.36, 95%CI:0.26-0.51), and 4) have temporary immigration status (2.1% versus 5.3%; OR=0.38, 95%CI:0.19-0.76). There were no differences by

racial/ethnic identity (p=0.11). Bisexual men used different websites and mobile apps; they used Squirt (81.7% versus 56.3%; OR=3.47, 95%CI:2.66-4.52) and Craigslist (49.1% versus 40.5%; OR=1.42, 95%CI:1.14-1.76) more, and Grindr less (28.1% versus 68.7%; OR=0.18, 95%CI:0.14-0.23). Bisexual men were less likely to have received sexual health information online (75% versus 85.3%; OR=0.49, 95%CI:0.38-0.64) and to have recently tested for STIs (45.4% versus 65.3%; OR=0.44, 95%CI:0.35-0.55). Bisexual men were more likely to report condom-use during their last male anal sex (65.7% versus 59.2%; OR=1.32, 95%CI:1.02-1.72). Among bisexual men, the only significant predictor of event-level condom use at last male anal sex was substance use (OR=0.50, 95%CI:0.29-0.88); where the partner was met, anal sexual position, HIV status concordance, and demographic factors were not significant predictors.

Conclusion: Ontario bisexual-identified MSM may have a distinct risk profile from other MSM supporting the need for targeted, culturally-relevant HIV prevention.

SS3.7

Assessing the Comprehensiveness of HIV Prevention, Treatment and Care Services for People Who Inject Drugs in Northern BC

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Background: The international community has had limited success in addressing HIV/AIDS among People Who Inject Drugs (PWID). This is of growing concern, particularly, in the northern, rural and remote regions, such as the western Canadian provinces where the rate of new infections among PWID remains high or has grown in opposition to stabilized or declining trends elsewhere. The purpose of this study was to determine the comprehensiveness of existing services for HIV prevention, treatment and care for PWID, specifically in northern BC and provide recommendations for updated service provision.

Methods: This project, using a Community Based Research (CBR) model, was completed in four phases: (1) mapping of existing services in northern BC, based on a Comprehensive Package listed in a 2012 WHO Technical Guide; (2) an adaptation of the WHO Guide to the northern BC context with the support of a Community Advisory Committee (CAC); (3) key informant interviews with three distinct populations - service users, providers, and decision-makers; and (4) development of a knowledge translation strategy.

Results: Results from the project included a detailed overview of current services based on information gathered through meetings with a 10 person CAC and interviews with 52 participants throughout northern BC. Key themes that emerged from analysis specific to the regional context, included: (1) service users are marginalized and face multiple challenges to accessing services; (2) service providers are limited in their capacity; (3) there is a general lack of awareness of services for PWID; (4) there is limited statistical information on HIV services for PWID; (5) there are communities in the region that have found innovative ways to provide services to PWID.

Conclusions: The final outcome of this exercise was a set of recommendations for implementing, monitoring, and stepping-up or scaling-down services for PWID in northern BC.

SS3.8

From One Ally to Another: Practical Guidelines to Better Include People who Use Drugs at Decision-making Tables

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Background: People who use illegal drugs are disproportionately affected by HIV and hepatitis C, stigmatization and social exclusion. To address these inequities, people who use drugs are increasingly included in decisions that affect them by sitting on policy, service delivery and research committees. This study addressed a gap in understanding how power inequities are transformed in committees where people who use drugs are at the table.

Methods: In partnership with the Drug Users Advocacy League and the Society of Living Illicit Drugs Users, this community-based participatory critical ethnographic inquiry explored power relations in four committees in two provinces. Data were collected in 2013 through observations at meetings, one-on-one interviews, demographics surveys and document reviews. Data analysis was guided by critical theory and transformative learning theory.

Results: Findings confirmed striking socioeconomic inequities between people who use drugs and others at the table. Inconsistent measures were taken by committees to alleviate barriers to inclusion. Despite openness to inclusion, committee members tended to underestimate the knowledge of people who use drugs. A structural environment that criminalizes people who use drugs fed stigma, which worsened inequities. Committees were committed to inclusion of people who use drugs; however, their capacity to do so varied due to constrained resources. The presence of local organizations of people who use drugs ensured a more democratic selection process of their representatives. At the table, a safe space was created by building trust, authentic relationships, dialogue, and skilled facilitation. Democratic practices of negotiated relationships and consensus-based decision-making enhanced meaningful inclusion.

Conclusions: Inclusion of people who use drugs can improve by planning ahead of time, implementing inclusive models at the table, catering to the specific needs of people who use drugs, practicing helpful facilitation skills, supporting organizations of people who use drugs and advocating on the social determinants of their health.

Poster Presentations – Présentation d'affiche

Basic Sciences

Sciences fondamentales

Co-Morbidities, Including HCV
Comorbidités, VHC compris

BSP1.01

Higher Plasma Cell-Free DNA with Younger Age and HIV Infection: Preliminary Results of a Cross-Sectional Observational Study

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Background: HIV infection and antiretroviral treatment are associated with mitochondrial dysfunction, cytotoxicity, and chronic inflammation. Increased cell-free nuclear (cf-nDNA) and mitochondrial (cf-mtDNA) DNA levels in the circulation are associated with poorer health outcomes, and cf-mtDNA is particularly pro-inflammatory given its resemblance to bacterial DNA.

Methods: Our observational cross-sectional study included 92 HIV+ (aged 4-63y), 45 HIV-exposed uninfected (2-18y), and 24 HIV-unexposed uninfected (15-78y) participants enrolled in the CARMA cohort study. The latter two groups were combined into one HIV- group. Fresh whole blood (WB) was centrifuged at 14,000xg and the plasma 0.45µm-filtered to remove cells and platelets. Total DNA was extracted from filtered plasma and corresponding WB, and both cf-mtDNA and cf-nDNA levels were quantified via multiplex qPCR.

Results: Within-participant cf-mtDNA were higher (median 6x) than cf-nDNA levels but the two were highly correlated in both groups ($r \geq 0.70$, $p < 0.0001$). No correlation was seen between cf- and WB DNA levels. Age was negatively correlated with cf-mtDNA and cf-nDNA in both the HIV+ (n=92, $rho \leq -0.26$, $p \leq 0.013$) and HIV- (n=69, $rho \leq -0.35$, $p \leq 0.004$) groups. HIV infection itself was associated with higher cf-mtDNA ($p=0.004$) and cf-nDNA ($p=0.003$) in pediatric participants (2-19y, n=72) but not in adults. In a multivariable linear regression model (n=161), younger age ($p<0.0001$) and HIV infection (HIV+ vs. HIV-; $p \leq 0.026$) were independently associated with higher cf-mtDNA and cf-nDNA. Among HIV+ participants, higher current $CD4^+$ T cell count was associated with higher cf-mtDNA and cf-nDNA (n=52, $r \geq 0.36$, $p \leq 0.009$). In a multivariable linear regression model of the HIV+ group (n=52), both younger age ($p \leq 0.009$) and higher $CD4^+$ count ($p \leq 0.019$) were independently associated with higher cf-mtDNA and cf-nDNA.

Conclusions: These data suggest that children have more circulating cf-DNA than adults, and that HIV+ persons have further increased levels. This could be related to aging processes and may contribute to chronic inflammation in HIV+ individuals.

BSP1.02

Validation of Multiplexed Quantum Dot-Barcode Diagnostic Technology to Detect HIV and Hepatitis B Virus Nucleic Acid

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Background: Nanotechnology represents a unique strategy to improve rapid point-of-care (POC) diagnostics, especially for multiplexing chronic, asymptomatic blood borne viruses such as HIV and hepatitis B virus (HBV). Moreover, while rapid HIV POC antibody testing is becoming more accessible globally, a positive HBV antibody test does not necessarily indicate infection. Thus, better diagnostic assays are needed. In Canada, a multiplex device would have wide applicability for front-line providers both at community health clinics working with marginalized and transient populations, or at rural and remote nursing stations. These cohorts may have increased exposure to HBV, reduced vaccine coverage, or may have weaning titers. The importance of knowing one's status cannot be understated, as co-infection may lead to more rapid disease progression, affect treatment decisions, and influence public health measures.

Methods and Results: Smartphones offer a unique avenue to implement POC HIV/HBV testing in resource-limited or remote areas. Here we validated quantum-dot barcode technology to detect HIV and HBV viral nucleic acid using a simple chip-based smartphone adapter developed in-house. We demonstrate the ability to detect HIV and HBV in clinical samples using a single-temperature, rapid amplification method, even in the presence of single-nucleotide polymorphisms. As HBV introduces additional diagnostic challenges including viral load and distinct genotypes, we subsequently tested 72 clinical samples to represent isolate diversity. We found that for HBV specifically, we are able to improve sensitivity by multiplexing target regions of the virus, in addition to multiplexing for co-infection.

Conclusions: Expanding treatment for both HIV and HBV into primary-care settings is the next step in addressing these diseases, but will only be possible if these infections are identified. Our tool has wide utility for assessing disease burden globally, and to improve identification and linkage to care for difficult to reach populations in Canada.

BSP1.03

Inflammation Accompanies Immune Senescence in Human Immunodeficiency Virus Infection

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While acute inflammation is important in immune responses to infection, chronic inflammation is pathological. Age-related morbidities prominent in chronic long-term human immunodeficiency virus (HIV) infection have pro-inflammatory components to their development.

Cytomegalovirus (CMV) infection creates an inflated CMV-specific CD8+ T cell population, often exaggerated in HIV infection. Perpetual activation and proliferation of CD8+ T cells potentially imposes a senescence-associated secretory phenotype. Senescent T lymphocytes characteristically: have short telomeres; express the terminal differentiation marker, CD57; lack the costimulatory molecule, CD28; and constitutively secrete pro-inflammatory molecules. We investigated whether chronic inflammation accompanied CMV infection and accumulation of senescent CD28-CD57+CD8+ T lymphocytes.

Plasma and peripheral blood lymphocytes were collected from 124 HIV-infected individuals and 33 age matched, apparently healthy controls. CMV-specific CD8+ T cell response and immunophenotypic CD28/CD57 expression levels were determined by flow cytometry. Serum levels of CMV-specific IgG, interleukin (IL)-1β, IL-6, tumour necrosis factor (TNF)-α, fractalkine (CX3CL1), and C-reactive protein (CRP) were measured by ELISA.

CMV-specific IgG and CMV-specific CD8+ T-cell responses correlated significantly with elevated inflammatory cytokine levels, particularly in subjects with higher percentages of CD57+CD8+ T cell populations. In HIV-infected and uninfected populations respectively, elevated levels of CX3CL1 ($p = 0.0004$, $p = 0.0301$) and CRP ($p = 0.0287$, $p = 0.0073$) in CMV-seropositive subsets, further supports linkages between CMV immunity, immunosenescence and inflammation. No significant correlations with age were observed, indicating aging itself has minor effects on immunosenescence and inflammatory markers in the context of chronic viral infection.

Our data supports an association between increased inflammation and immunosenescence in chronic HIV infection. Understanding mechanisms behind senescence-associated chronic inflammation, including the role of CMV infection, could introduce new strategies for preventing age-related morbidities.

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BSP1.04

Hepatitis C virus core protein reduces CD8+ T-cell proliferation and perforin production

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Background: Clearance of HCV is dependent on an effective $CD8^+$ T-cell response and dysfunction of HCV-specific $CD8^+$ T-cells has been widely observed in chronic infection. We and others have also observed impaired functionality of bulk or non-HCV specific $CD8^+$ T-cells in chronic HCV mono- and HIV-HCV co-infection. This may contribute to observed reductions in immunity to other pathogens, including HIV, and the increased prevalence or accelerated disease progression of extra-hepatic diseases dependent on effective $CD8^+$ T-cell responses (e.g. viral co-infections, cancer) in HCV-infected individuals. Evidence suggests that HCV core protein may contribute to this dysfunction, and its circulating levels are elevated in chronic disease.

Method: To study this dysfunction, isolated human $CD8^+$ T-cells from healthy donors were pre-incubated with recombinant HCV core protein for 72 hours and then stimulated accordingly to evaluate proliferation, cytokine signaling, degranulation and the production of Bcl-2, perforin and IFN-γ by flow cytometry.

Results: Pre-incubation with HCV core significantly reduced the proliferation of $CD8^+$ T-cells. Perforin production and degranulation was also decreased in cells pre-treated with HCV core while IFN- γ production remained unchanged. Bcl-2 production in response to cytokine stimulation in cells pre-incubated with HCV core was similar to cells treated with cytokine only, but pSTAT5 production (required for Bcl-2 production) was increased.

Conclusion: Our study reveals that HCV core reduces the activity and target lysis-associated functions of $CD8^+$ T-cells, suggesting a functional anergy. This may contribute to the generalized impairment of $CD8^+$ T-cells observed in chronic HCV mono- and HIV-HCV co-infection, providing insight for the design of novel counteractive immune-mediated strategies including the design of effective therapeutic vaccines. Particularly, if increased STAT5 activation can be exploited, a modified core protein may play a role in improving vaccine efficacy.

BSP1.05

Immunological Investigation into HIV/Mycobacterium tuberculosis co-Infection and Disease

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HIV-infected individuals are 25-50 times more likely to develop active tuberculosis (ATB). This increase in ATB and the subsequent increased mortality is likely due to the immune defects from HIV infection. These defects reduce the sensitivity of *Mycobacterium tuberculosis* (Mtb) diagnostics. The current gold standard interferon-γ release assay (IGRA) immunodiagnostic relies on Mtb antigen-specific IFNγ release in whole blood. We use this assay in our studies as a comparator to define alternate immunological signatures to Mtb in HIV co-infection in order to identify targets that might increase the sensitivity of this diagnostic in that group.

We hypothesize that the immune deficiencies resulting from HIV-infection will affect multiple TB-specific immune responses and describe differential TB responses between HIV+ and HIV- Kenyans with and without ATB. We hope to find alternate markers of ATB in an attempt to ameliorate the current IGRA.

We performed the IGRAs in HIV+ and HIV- individuals with or without ATB from Nairobi, Kenya. This diagnostic test relies primarily the CD4+ T cell IFNγ responses in whole blood to Mtb-specific antigens. Through multiplexed chemokine and cytokine assays of the stimulation supernatants, we define the immune perturbations in HIV/TB co-infection. There is a general decline in soluble responses to Mtb antigen stimulation of whole blood among ATB participants. As CD4 declines, there is a notable loss of certain but not all cytokine responses to Mtb antigens, and in fact there may be soluble factors that increase the sensitivity of TB diagnosis in HIV co-infection.

This study is the first to define a broad range of immunological responses to Mtb-specific antigens in HIV-co-infected individuals. It creates a foundation to further study of putative biomarkers of ATB in HIV-infected individuals. Additionally, we have contributed greater understanding of immunity to TB in this high-risk population.

HIV Immunology
Immunologie du VIH

BSP2.01

IL-32 is a Reliable Biomarker for HIV Disease Progression

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Background: Persistent immune activation in HIV infection is a major driver of CD4 T-cell depletion and immune dysfunction. Subjects who naturally control HIV infection in the absence of treatment, HIV-infected slow progressors (SP), show residual immune activation, which could promote disease progression. We investigated the role of inflammatory factors in HIV progression in subjects who maintained slow progression status without treatment for several years before losing disease control.

Methods. We identified n=5 subjects within our Canadian Cohort of HIV$^+$ Slow progressors (CTN 247) who experienced loss of VL control (@20 fold increase in VL) and a decline in the absolute CD4 counts (@211 cells/mm^3). Transcriptional analysis by microarray using the Illumina BeadChip was carried out on PBMCs isolated from these subjects before and after loss of control. Modulated inflammatory factors identified by microarray analysis were validated by direct ELISA on plasma of SP at two time intervals (mean 30 ± 19 months).

Results: By applying a cut-off value of a 1.3-fold change in gene expression before and after loss of control, we identified 207 significantly down-regulated genes and 83 up-regulated genes. Among the most significantly down-modulated genes we identified the less inflammatory isoforms of the novel cytokine IL-32 (IL-32a and IL-32d). Validation on plasma from HIV-infected SP subjects (n=53) showed that while there was a significant decrease of IL-32a this was coupled with increase in the proinflammatory isoforms of IL-32, mainly IL-32g. Levels of IL-32-non-alpha isoforms at the first time point positively correlated with the decline of CD4 T-cell counts, increased VL, lower CD4/CD8 ratio and levels of inflammatory markers (sCD14 and IL-6) at the later clinic visit.

Conclusions: Proinflammatory isofoms of IL-32 realibly predict disease progression in HIV-infected SP. IL-32 is worth investigating as a biomarker for HIV progression and a potentially therapeutic target in HIV infection.

BSP2.02

Assessment of the LAG-3 Inhibitory Mechanism on T cell Activation

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Background: An HIV functional cure would restore the immune response such that after stopping antiretroviral therapy, HIV does not rebound. Immune exhaustion describes an immunodeficiency that is a direct consequence of persistent immune activation. LAG-3 is an exhaustion marker expressed on lymphocytes in cases of persistent activation, including during HIV infection. LAG-3 is elevated on NK, iNKT and T cells during HIV infection, is associated with dysfunction of these cells and its expression correlates with HIV disease progression and rapid viral rebound. Like other exhaustion markers, LAG-3 likely contributes to the exhaustion phenotype through inhibition of lymphocyte activation.

Rationale: T cell receptor (TCR) signaling occurs via a phosphotyrosine pathway. Calcium influx is a critical pathway component for complete T cell activation. LAG-3 activity impairs calcium flux, proliferation and cytokine production following T cell stimulation, but the mechanism and differential effects on cell subsets are largely unknown. LAG-3 binds MHC II and localizes to the immune synapse during stimulation, suggesting influence on proximal TCR signaling.

Hypothesis: LAG-3 inhibits phosphorylation of a proximal TCR signaling protein during T cell stimulation, exerting similar effects on all T cell subsets.

Approach: Using phospho-microarray and phospho-flow cytometry compared the phosphorylation state of TCR signaling proteins following CD3 stimulation with or without LAG-3 cross-linking, and SEB stimulation with or without LAG-3 blockade. In this manner we determined whether and at which stage LAG-3 impacts the TCR pathway by deducing the earliest signaling protein to differ between conditions. Also using flow cytometry, we analyzed cytokine production between common T cell subsets following SEB stimulation with or without LAG-3 blockade.

Significance: Determining the LAG-3 mechanism and its potential differential functions on subsets allows inference of its situational importance and may lend credence to novel therapeutic strategies for a functional HIV cure.

BSP2.03

Reducing endogenous IRF-7 expression limits transactivation of HIV-1 genes in primary human CD4+ T cells

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Introduction: Interferon regulatory factor-7 (IRF-7), the "master regulator" of type 1 interferon, has been shown to regulate anti-viral immune responses. IRF-7 expression can be upregulated during HIV-1 infection and has been implicated in anti-HIV-1 interferon responses. Nevertheless, the role of IRF-7 in HIV-1 infection remains controversial, perhaps due to different cell types used in the studies. Here, we examined IRF-7 expression in major PBMC subsets, and assessed the hypothesis that reducing cellular IRF-7 will render ex-vivo CD4+ T cells more susceptible to infection.

Methods: IRF-7 level was examined using multi-color flow-cytometry, and modulated by transfection with siRNA or transduction with shRNA containing lentivirus in ex-vivo CD4+ T cells. The effects of IRF-7 knockdown on transactivating HIV-1 gene efficiency was assessed using p24 ELISA and flow cytometry.

Results: In unstimulated PBMC, IRF-7 was constitutively expressed in every cellular subtype we examined (CD4, CD8, B-cells, NK cells, monocytes, and dendritic cells), with the highest expression found in monocytes and dendritic cells ($n=18$, $p \leq 0.0001$). In response to exogenous interferon-alphaA (5000 U/ml), IRF-7 protein level was increased by ~2-fold ($n=18$, $p \leq 0.001$) in all cellular subtypes. During HIV-1 infection, IRF-7 expression was upregulated ~2 fold ($p \leq 0.0001$), in the infected cell subset at 96 hours post-infection. We saw no correlation between the degree of IRF-7 knockdown and the extent of inhibition of p24 transactivation. However, contrary to our hypothesis, we consistently observed less p24+ cells with IRF-7 knockdown.

Summary: Although IRF-7 is constitutively expressed in all cell subsets we examined, significantly higher IRF-7 expression in monocytes and dendritic cells suggests these cell types may be critical in early IRF-7 mediated interferon responses. Furthermore, this is one of the first studies suggesting that IRF-7 plays a critical role in HIV-replication in CD4+ T cells, a major HIV target.

BSP2.04

Effect of Sex Work on the Vaginal Microbiome in a Cohort of Women from Nairobi, Kenya

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Background: The vaginal microbiome and the immune system maintain a homeostatic balance within the female genital tract under normal healthy conditions. Studies indi-

cate that a "healthy" vaginal microbiome is dominated by *Lactobacilli spp.*, and dysbiosis of the vaginal microbiome is correlated with bacterial vaginosis and increase in inflammation that enhances the risk of HIV-1 acquisition. Ethnic differences have been noted in the dominant vaginal bacterial species and in women of non-Caucasian origin, especially Black women, clinical symptoms do not consistently match the current definition of "healthy" microbiome or bacterial vaginosis.

Methods: In the current study, we compared high risk sex workers from the Pumwani clinics in Nairobi, Kenya, with women from the same community not involved in sex work (lower-risk), to determine the profile of vaginal microbiome and determine how sex work may alter it. Genomic DNA was extracted from CVL samples of 20 sex workers and 9 lower-risk women and the V3 region of the 16S rRNA was amplified by PCR and sequenced using the Ilumina MiSeq platform and an in house bioinformatics pipeline was used to determine the bacterial species and their relative abundance.

Results: Initial results showed a significant difference in relative abundance of Lactobacillus spp. between sex workers and lower-risk women, with 25% of sex workers showing >45% relative abundance of *Lactobacillus spp* compared to 67% of lower-risk women. Clinical diagnosis of BV among sex workers was associated with presence of polymicrobial bacterial species, including those typically associated with BV such as *Prevotella* and *Gardnerella*.

Conclusion: The results indicate that sex work is likely associated with alternations in the vaginal microbiome. Ongoing studies are examining how the vaginal microbiome is altered by hormonal contraceptives in sex workers and lower-risk women.

BSP2.05

Inducing immune quiescence to reduce the number of HIV target cells in the female genital tract does not suppress the local innate immune response

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Background: With over 2 million new HIV infections occurring annually, new HIV prevention approaches are needed. As immune activation/inflammation is known to be a risk factor for HIV acquisition, we administered daily oral low doses of anti-inflammatory agents and determined that they could reduce the number of HIV target cells (CCR5+ CD4+ T cells) in the female genital tract. However, the impact of the use of oral anti-inflammatory agents on the local innate mucosal immune response has not been determined.

Methods: Daily oral administration of low doses of acetylsalicylic acid (ASA) (81mg) and hydroxychloroquine (HCQ) (200mg) were taken daily for 6 weeks. Samples of blood and cervicovaginal lavage (CVL) were taken pre- and during drug administration. The innate immune response was assessed by determining the level of 23 (?) cytokines and chemokines in plasma and CVL.

Results: In this study, we showed no change in the expression of innate cytokines and chemokines (IL-15, IL-1a, IL-1b, IL-8, IP-10. MCP-1, MIP-1a, MIP-1b, MIP-3a) following initiation of drug therapy in both at the systemic and mucosal compartment.

Conclusion: Herein, we showed that the use of anti-inflammatory agents that resulted in a reduced number of HIV-target cells, did not have a detrimental effect on the innate immune response as determined by assessing cytokines and chemokines. This preliminary data indicates us that inducing immune quiescence does not lead in an immunosuppression of the immune system. Further studies assessing the impact on the adaptive immune response a pre and during IQ induction by HCQ or ASA are needed.

BSP2.06

The effect of depot medroxyprogesterone acetate (DMPA) on the mucosal immune system in the female genital tract: implications for HIV risk

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Background: Depot medroxyprogesterone acetate (DMPA) is an injectable progesterone-based contraception that is used worldwide, including areas of high HIV incidence. However, the possibility that DMPA increases risk of HIV acquisition has been raised and is a major global health concern Therefore, it is important to determine how DMPA might impact the female genital tract immune system and the effect that could have on HIV acquisition risk.

Method: Female sex workers from Nairobi, Kenya, using DMPA (n=15) and those not using any hormonal contraception (n=33) were recruited and followed for a period of 3 months. Cervico-mononuclear cells (CMC), cervico-vaginal lavage (CVL) and cervical biopsy were taken.

Results: Preliminary results indicates that at the first study visit women using DMPA had a more pro-inflammatory environment as determined by elevated level of IFN-g (p=0.03), IL-10 (p=0.05), IL-12 (p=0.02), IL-15 (p=0.03), IL-17A (p=0.04), IL-2 (p=0.01), MIP-3a (p=0.003). The expression of MIP-1b and sIL2RA also trended to be higher in the CVL of women using DMPA compared to women not using hormonal contraception. Consistent with an inflammatory environment, women using DMPA had elevated levels of CD69+ on CD4+ T cells (p=0.02) and CD8+CCR5+ T cells (p=0.03) in the CMC. Analysis of cervical biopsy is ongoing and will provide an understanding of where in the cervix

are located the HIV target cells and if results from CMCs analysis can be extrapolated to the endocervical tissue.

Conclusion: This study demonstrates that the use of DMPA leads to a pro-inflammatory environment at the female genital tract, which could have implication for increasing the risk of HIV infection.

BSP2.07

Dynamics of antibody-mediated neutralization and ADCC response in HIV-positive individuals under suppressive antiretroviral therapy

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Dolutegravir (DTG) is the newest and most potent member of the integrase inhibitors on the market. No reports of drug resistance have been reported in patients receiving first-line DTG treatment since its FDA approval in 2013. The implication of the lack of resistance is immense, and 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 response against HIV-1 will shed light on the status of viral infection during suppression achieved by antiretroviral (ARV) therapy.

Essential immune responses against HIV-1 include the production of antibodies. Neutralizing antibodies bind and prevent HIV-1 from infecting new cells, and non-neutralizing antibodies may mediate antibody-dependent cellular cytotoxicity (ADCC), whereby immune effector cells lyse HIV-1 infected cells upon antibody binding to HIV-1 antigens on target cell surfaces.

Our study is a longitudinal observational study. Serum samples were obtained from patients treated with combinations of different ARVs including DTG plus emtricitabine (FTC) and tenofovir disoproxil fumarate (TDF), DTG plus abacavir (ABC) and lamivudine (3TC), elvitegravir/cobicistat plus FTC and TDF, raltegravir plus ABC and 3TC, efavirenz plus FTC and TDF, and darunavir/ritonavir plus FTC and TDF. Neutralization assays in TZM-bl cells and ADCC assays in CEM CCR5+ Luc+ cells were performed using two samples per patient. The first samples were selected from patients after initial viral suppression and the second samples were obtained 9-17 weeks after the initial sample. The neutralization titre (relative serum dilution) and ADCC-mediating potency of the serum samples were measured.

Our results reveal the evolution over time of antibody-mediated neutralization and ADCC responses in HIV-positive individuals who are successfully treated with combination ARV therapy.

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BSP2.08

Dichotomous Relationship of TLR7 and TLR8 Responses in HIV Exposed Seronegative Sex-Workers and Its Linkage to HIV Susceptibility in vitro

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Identifying the correlates of innate immune protection against Human Immunodeficiency Virus is an important goal for development of effective anti-HIV therapies and vaccines. Not all exposures to HIV end in infection. The innate immune system is at the interface between the host's immune system and initial contact with HIV.

This study compared the Toll-like receptor responsiveness of different immune cells from the peripheral blood mononuclear cells (PBMCs) of HESN and HIV negative (susceptible) commercial sex workers (CSWs), to TLR4 (bacterial cell wall lipopolysaccharide-LPS), TLR7 (Imiquimod) and TLR8 (single stranded RNA-ssRNA). HESN had a hypo-responsiveness to TLR4 and TLR7 ligands, but hyper-responsiveness to TLR8 following stimulation with ssRNA analogous to HIV's, evidenced by reduced cytokine responses to both TLR4 and TLR7 stimulation, but higher responses to TLR8 stimulation in HESN PBMCs. The 'dichotomy' in TLR responsiveness of HESN PBMCs was associated with differential expression of cognate TLRs on PBMCs and altered activation of TLR signalling pathways. The opposing pattern of TLR7 and TLR8 responsiveness correlated with the ability of HIV to infect target cells *in vitro*; where pre-treatment of PBMCs with TLR7 enhanced HIV replication while TLR8 stimulation inhibited HIV replication. These differences in outcomes of the *in vitro* HIV infection assays were associated with distinct cytokine profiles whereby TLR7 stimulation induced robust type I IFNs responses without proinflammatory TNF-α and IL-12 cytokine responses, while TLR8 stimulations led to type II IFN responses accompanied by robust proinflammatory responses in both groups.

These results demonstrate that the lower or 'quiescent' activation state in HESN PBMCs, did not affect the innate immune response to RNA analogous to HIV derived genetic material and capable of limiting HIV infection *in vitro*. These findings contribute to the growing knowledge on TLR7 and TLR8 responses particularly in relation to HIV infection,.

BSP2.09

Interruption of sex work has subtle effects on systemic immune activation in sex workers from Nairobi, Kenya

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Background: Unprotected sexual intercourse exposes the female genital tract to semen-derived antigens, which leads to an inflammatory response. Studies have shown that this post-coital inflammatory response can lead to recruitment of activated T cells to the FGT, which may increase risk of HIV infection. The objective of this study was to evaluate the impact of sex work on activation and memory phenotype of peripheral T cells among female sex workers (FSW) from Nairobi, Kenya.

Subjects: Thirty FSW were recruited from the Pumwani Sex Workers Cohort; 10 in each of the following groups: HIV-Exposed Seronegative (HIV-negative with at least 7 years in active sex work), HIV-positive, and New Negative (HIV-negative, less than 3 years in active sex work). Blood was obtained at three different phases; active sex work, during a break from sex work, and following a return to sex work. The break from sex work was to allow the women to heal following cervical biopsies. PBMCs were stained for phenotypic markers (CD3, CD4, CD8, and CD161), memory phenotype markers (CD45RA and CCR7), activation markers (CD69, HLA-DR, and CD95) and HIV co-receptor (CCR5). T cell populations were compared between groups.

Results: In the HIV positive group, CD8+CCR5+ T cells declined ($p < 0.01$) while CD4+CD161+ T cells trended to increase ($p=0.054$) and CD4+ terminally differentiated cells increased ($p=0.03$) during the sex break. In the New Negative women, there was a modest trend for a decrease in naïve CD8+ T cells ($p=0.09$) over time. Independent of sex work, HIV-positives had higher effector memory ($p < 0.01$) and CD8+CD95+ T cells ($p < 0.01$) and lower naïve CD8+ T cells ($p < 0.01$) than other groups.

Conclusions: Interruption of sex work had subtle effects on systemic T cell activation and memory phenotypes suggesting that exposure to sex antigens could affect peripheral immune cells.

BSP2.10

Depot Medroxyprogesterone Acetate Increases T cell Activation Markers in the Female Genital Tract

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Background: Depot Medroxyprogesterone (DMPA) is one of the most widely used contraceptives in the world. However, there is growing debate on its relationship with susceptibility to HIV in the female genital tract. There is need to explore the effect of DMPA on T cell activation.

Objective: To evaluate the effect of DMPA on T cell activation at the systemic compartment.

Methods: Fifteen female sex workers (FSW) using DMPA and 33 FSW on not on any hormonal contraception were recruited. Blood was obtained from all participants. Baseline expression of CD69, HLA-DR, CD95, CD161 and CCR5 on peripheral blood mononuclear cells was assessed and compared between the two groups.

Results: The expression of CD69 and CD95 was significantly elevated on both CD4 (respectively $p<0.0001$ and $p=0.007$) and CD8 T cells ($p=<0.0001$ and $p=0.005$) in women using DMPA as a contraceptive method versus women not using hormonal contraception. The frequency of CD8+HLA-DR+ T cells was also increased in women using DMPA. In this study, we also demonstrated that DMPA modifies the leucocyte trafficking as the cytokine/chemokine ratio (plasma/mucosal) was altered in the women on DMPA group. Indeed, in women using DMPA, the ratio of IL-8 ($p=0.05$), MIP-3a ($p=0.01$), Il2RA ($p=0.009$), sCD40L ($p=0.05$), IL-12 ($p=0.005$) and IL-17A ($p=0.005$) was significantly lower than the ratio observed in women not using hormonal contraception. This indicates a higher production of those cytokines/chemokines at the mucosal compartment.

Conclusion: This study showed that the systemic compartment is significantly affected by exogenous progesterone resulting in increased expression of activation markers on potential HIV target cells. Further studies will assess the mucosal compartment.

BSP2.11

Retinoic acid-mediated imprinting for gut homing renders Th17 cells highly permissive to HIV-1 infection by modulating the mTORC1 pathway

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Background: HIV-infected CD4+ T-cells are enriched in gut-associated lymphoid tissues. Retinoic acid (RA), a vitamin A metabolite, induces imprinting for gut-homing. We previously demonstrated that CD4+ T-cells expressing the Th17 marker CCR6 are permissive to HIV *in vitro*, harbor HIV reservoirs in ART-treated subjects, and that RA increases HIV replication in these cells. To identify RA-induced HIV dependency factors, we performed a genome-wide transcriptional profiling in RA-treated CCR6+ *versus* CCR6- T-cells.

Methods: CD4+ T-cells were sorted from PBMCs using magnetic beads (Miltenyi). Memory (CD45RA-) CCR6+/CCR6- T-cells were sorted by FACS (BDAriaII). Cells were stimulated *via* CD3/CD28 and cultivated in the presence/absence of RA (10nM). Total RNA was extracted for microarrays analysis (Illumina). Validations of microarrays were performed by real-time PCR and/or FACS. HIV-DNA integration was measured by real-time PCR. RA-treated cells were exposed to HIV in the presence or absence of mTORC1/2 inhibitors. HIV-DNA integration was measured by real-time PCR. Levels of HIV-p24 by ELISA and FACS. Cytokines were quantified by ELISA.

Results: Among "*present calls*", 1,538 and 1,285 were modulated by RA in CCR6- and CCR6+ T-cells, respectively (*p-value* <0.05). Gene Set Variation Analysis and Ingenuity Pathway Analysis identified the mTORC1 pathway as modulated by RA in CCR6+ T-cells. RA-mediated mTOR upregulation in CCR6+ T-cells was confirmed by western blotting. Exposure to Rapamycin (mTORC1 inhibitor) and INK128 (mTORC1/2 inhibitor) counteracted the effect of RA on HIV replication in CCR6+ T-cells without interfering with their Th17 effector functions.

Conclusions: Our studies demonstrate that RA-mediated imprinting for gut-homing is associated with increased HIV permissiveness in CCR6+ but not CCR6- T-cells and reveal mTORC1-mediated mechanism underlying these differences. Our findings support the use of mTORC1/2 inhibitors as a new therapeutic strategy aimed at limiting HIV permissiveness in gut-homing Th17 cells, as well as the restoration of mucosal immunity in HIV-infected subjects.

BSP2.12

The Effects of Oxytocin on the Immune Cytokine Profile of Vaginal, Ectocervical, and Endocervical Epithelial Cells

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Introduction: Oxytocin is a neurohypophyseal peptide that is associated with social bonding, contraction of the uterus, and, recently, modulation of immune activation. However, little is known of how oxytocin boosts immunity, and whether repeated exposure to oxytocin would alter cellular susceptibility to infection. This study will investigate whether the immunomodulatory effects of oxytocin would be sufficient to create a quiescent immune environment, unfavourable to the establishment of HIV infection.

Methods: Epithelial cell lines of vaginal (Vk2), ectocervical (Ect1), and endocercival (End1) origins will be cultured in the presence of oxytocin (0.2-20 000 pg/mL) to capture physiological and supra-physiological doses. They will be treated for 15 minutes, 30 minutes, 1 hour, 2 hours, and 4 hours to allow for the analysis of rapid and later signalling events. RNA, cells, and culture supernatants will be collected for gene expression analysis, flow cytometry, and cytokine assays, respectively.

Pro-inflammatory genes/markers: eIF2a, G-CSF, GM-CSF, IL-1β, IL-6, IL-8, MCP-1, MIP-1α/β, NF-KB, PERK, PKR, TNFα, Anti-inflammatory genes/markers: IKB, peIF2a, PGE2, pPERK, pPKR

Anti-viral genes/markers: Elafin, HBD2, RANTES, SLPI

Signalling molecules: eIF2a, IKB, NF-KB, peIF2a, PERK, PKR, pPERK, pPKR, OXTR

Expected Results: We expect production of anti-inflammatory mediators, and decreases in the secretion of pro-inflammatory cytokines/chemokines upon exposure to oxytocin in a dose dependent manner. These anti-inflammatory mediators are expected to reduce the levels of immune-activation at the female genital tract (FGT), and decrease potential HIV-targets, such as activated CD4+ T cells at the FGT.

BSP2.13

The Testis as an Immune Privileged site and its contribution to HIV Persistence: Assessing Myeloid-Derived Suppressor Cell distribution

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Background: The testis constitutes a significant HIV reservoir in ART-treated subjects. Testes have a distinctive role in protecting immunogenic spermatids from innate and adaptive immune responses, establishing an immune privileged site. Such immune privilege may result in HIV persistence. We previously reported on a high frequency of $CD39^+$ regulatory T cells in testes as compared to blood in ART-treated individuals. Herein, we assessed two methods to identify testicular myeloid-derived suppressor cells (MDSCs), a subgroup of myeloid cells contributing to immunosuppression.

Methods: Testes and blood samples from ART-treated and control individuals who elected to have gender reassignment surgery were processed immediately after intervention. Pieces of tissue were fixed before paraffin embedding to analyze tissue architecture and immune cell distribution by optic microscopy. A leukocyte-enriched suspension was obtained using either mechanical disruption or enzymatic digestion of the tissue, followed by magnetic $CD45^+$ cell sorting. Granulocytic ($CD15^+$) and monocytic ($CD14^+$) MDSCs ($HLA\text{-}DR^{-/lo}CD33^{hi}CD11b^{hi}$) were assessed in testicular cell suspension and PBMC using flow cytometry.

Results: Tissue architecture was well preserved and lymphoid and myeloid cells localized in the interstitial space in testes of HIV-infected and control individuals. En-

zymatic digestion of the tissue followed by a decantation step resulted in interstitial $CD45^+$ leukocyte enrichment, as compared to mechanical disruption (respectively 10% and 3% of total testicular cells, n=2). $CD45^+$ cell sorting was required for flow cytometry phenotyping of MDSCs. In one uninfected subject, MDSCs represented 2.5% of HLA-$DR^{-/lo}$ testicular myeloid cells, compared to 11% in the blood. In this subject, $CD15^+$ granulocytic MDSCs constituted 47% of testicular MDSCs.

Conclusions: This is the first identification of MDSCs in the human testis. Future studies will assess MDSC immunosuppressive functions and their relation with the frequency of HIV-infected cells in the tissue, and will contribute to a better understanding of HIV persistence in immune privileged sites.

BSP2.14

Systemic Inflammation before and after antiretroviral therapy initiation as a predictor of immune response among HIV-infected individuals in Manitoba

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Introduction: It is known that in in spite of treatment with HAART, and subsequent viral load suppression, HIV-positive individuals are likely to endure persistent immune system activation. What remains unknown is whether chronic subclinical inflammation itself is related to impaired immune recovery following commencement of ART, and as a result, undesirable outcomes.

Methods: Ten HAART-naïve patients enrolled in the Manitoba HIV program were followed for an average of one year. Plasma samples were obtained at 4 timepoints an average of 3 months apart, commencing prior to initiation of HAART, and ending with the achievement of complete viral suppression. Plasma concentrations of 38 markers of inflammation were measured using cytokine bead arrays; we then compared whether there was any significant difference in inflammation marker levels in patients with "good" vs. "poor" CD4+ cell count recovery (defined by WHO criteria for immunological failure.)

Results: In our cohort, IL-11, IL-20, INF-a2, APRIL, Osteocalcin, and TSLP remained persistently high in patients with suboptimal immune recovery compared to those with optimal immune recovery, or became elevated over time in those with poor immune recovery. Chitinase 3-like-1, sIL-6, IL-28A, and sTNF-R2 were initially elevated in those that ultimately demonstrated poor immune recovery, but matched levels of those with good immune recovery group after one year.

Conclusion: Chitinase 3-like-1, sIL-6, IL-28A, and sTNF-R2, markers that were elevated in the poor recovery group only at the first timepoint, may have utility as early predictors of suboptimal immune recovery.

Furthermore, in MB HIV patients, several markers of inflammation either remained persistently high in those with suboptimal immune recovery compared to those with optimal immune recovery, or became elevated in those with poor immune recovery: IL-11, IL-20, INF-a2, APRIL, Osteocalcin, and TSLP. These biomarkers could potentially serve as markers of inadequate immune response and targets for ancillary therapies to HAART.

BSP2.15

Immunologic non-response during HIV infection is associated with increased immune activation and markers of intestinal damage

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Introduction: Despite viral suppression on effective antiretroviral therapy (ART), individuals living with HIV have elevated immune activation, driven in part by bacterial translocation across an impaired gut barrier. Whether these alterations are more pronounced in individuals on ART who achieve viral suppression but fail to recover CD4 T cell numbers in blood, so-called "immunologic non-responders" (INR), is not clear. We measured levels of immune activation in INR individuals, and examined associations with plasma markers of gut damage and microbial-related immune activation.

Methods: Twenty participants were recruited through the Maple Leaf Medical Clinic in Toronto: (1) INRs (n=14), defined as a CD4 T cell count $<350/mm^3$ despite >2 years viral suppression on ART; and (2) community-matched HIV-negative individuals (n=6). Blood CD8 T cell immune activation (%HLA-DR+CD38+) was assessed by flow cytometry. Plasma markers of gut epithelial damage and immune activation (I-FABP, sCD14 respectively) were quantified using ELISA.

Results: INR individuals had elevated blood CD8 T cell immune activation compared to HIV- controls (2.2% vs. 0.57%; $p<0.01$). Further, INRs had a reduced CD4/CD8 ratio ($p<0.01$), which negatively correlated with blood immune activation (Spearman r=-0.5845; $p<0.01$). INRs had elevated plasma markers of gut damage and monocyte activation compared to controls (677.4pg/mL vs. 334.1pg/mL I-FABP, 1.697mg/mL vs. 1.348mg/mL sCD14; $p<0.02$).

Conclusion and Future Directions:

Elevated plasma markers of intestinal damage and microbial-associated immune activation suggest that intestinal immunopathology may drive immunologic non-response. Further comparisons to HIV+ immune restorers (n=14), defined as HIV+ individuals with a nadir CD4 T cell count $<350/mm^3$ and restoration to $>350/mm^3$ on ART, are near completion to reveal whether immune non-response is disproportionately linked to gut immunopathology and immune activation. Together these findings suggest that

mitigating immune activation-associated health burdens during immunologic non-response may require gut-targeting interventions.

BSP2.16

Plasma Antibodies to HIV-1 Protease Cleavage Sites and HIV Infection

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Background: HIV-1 protease cleavage sites (PCS) are a novel target for an HIV vaccine, as disruption of the cleavage process may lead to non-infectious virus. Previously, we have studied anti-HIV PCS CD8+ T cell responses in the Pumwani cohort. The focus of this study is to investigate plasma antibodies to HIV-PCS and their role in HIV infection in the Pumwani sex worker cohort.

Methods & Materials: Plasma samples of sex workers enrolled in the Pumwani sex worker cohort in Nairobi, Kenya were screened for antibodies against PCS peptides and two non-PCS peptides (1 Gag and 1 Env) using a multiplex assay with the Bio-Plex 200 system. The results were analyzed using Student's *t*-test and Bonferroni correction with SPSS 22.0 and GraphPad 5.01.

Results: Preliminary analysis of 111 samples (41 HESN, 38 HIV- and 32 HIV+) showed that antibody responses against PCS-6 (P=5.6x10^{-4}, *adj. P*=0.0085) which cleaves p7(NC)/TFP, PCS-11 (P=7.6x10^{-7}, *adj. P*=1.1x10^{-5}) which cleaves p66(RT/RNase)/IN, and Gag (P=1.3x10^{-4}, *adj. P*=0.0019) were significantly higher in HESN individuals compared to the HIV negative group.

Conclusion: We identified many differences in the antibody responses against HIV-PCS peptides, Env, and Gag between HESN, HIV negative, and HIV positive individuals within the Pumwani sex worker cohort. The higher antibody responses observed in HESN individuals compared to the HIV negative group indicate the possibility that these antibodies are involved in protection against HIV infection and warrants further investigation.

BSP2.17

Activating Natural Killer (NK) Receptor (aNKR) Ligand Profile of HLA-Null and HIV-1 Infected CD4+ T Cells

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Background: HIV-infected CD4 T cells (iCD4) activate NK cells to inhibit HIV replication. Whereas the impact of the interaction of inhibitory NK receptors (iNKR) with their HLA ligands on iCD4s on NK cell activation has been investigated, the contribution of interactions between aNKR and their ligands on iCD4 to NK cell activation is less well described. Furthermore, the HLA-null cells 721 and K562 stimulate NK cells differentially likely due to differences in their expression of aNKR ligands. Here, we characterized iCD4 and HLA null cells for expression of a set of aNKR ligands.

Methods: CD4$^+$ T cells from 8 HIV-1 seronegative donors were activated and infected with $HIV_{JR\text{-}CSF}$ for 7 days or left uninfected (unCD4) as controls. CD4$^+$, K562, and 721 cells were stained with antibodies (Abs) to ULBP-1, ULBP-2/5/6, ULBP-3, HLA-E, and ICAM-1. CD4$^+$ cells were stained for intracellular p24 and cell surface CD3 and CD4 to distinguish p24$^+$CD4 that had or had not downregulated CD4 (iCD4$^+$, iCD4$^-$) from exposed uninfected CD4 (euCD4).

Results: The frequency of 721 cells expressing ULBP-1, ULBP-2/5/6, ULBP-3, HLA-E, ICAM-1 was 0.8, 0.1, 5.6, 65.7, and 97.5%, respectively. The frequency of K562 expressing these ligands was 0.2, 70.0, 2.1, 5.2, and 93.2%, respectively. A higher frequency of iCD4 than unCD4 expressed each of these ligands ($p \leq 0.0391$ for all, Friedman tests). EuCD4 and unCD4 expressed these ligands at similar frequencies. Fewer iCD4$^-$ than iCD4$^+$ expressed these ligands ($p \leq 0.023$ for all, Friedman tests).

Conclusions: HIV infection of CD4 cells upregulates the expression the aNKR ligands screened for. Some of these ligands may be downregulated in parallel with CD4, as the frequency of iCD4 expressing these ligands is lower in the CD4$^-$ than the CD4$^+$ iCD4 subsets. We observed a higher frequency of HLA-E$^+$ 721 than K562 cells and a lower frequency ULBP-2/5/6$^+$ 721 than K562 cells.

HIV Molecular Epidemiology, Including Host Genetics and HIV Evolution
Épidémiologie moléculaire du VIH, y compris la génétique des hôtes et l'évolution du virus

BSP3.01

Expression Profiling Of Key Genes Involved In Glucose Metabolism in HIV Highly Exposed Yet Seronegative Commercial Sex Workers, Nairobi, Kenya

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Introduction: Cellular metabolism regulates immune cell functions and differentiation, thereby affecting im-

mune response. (Jacobs, et al, 2008) Activated T cells have increased metabolic requirements. (Fox *et al*, 2005; MacIver *et al*, 2008) Aerobic glycolysis is required by proliferating T cells to meet the metabolic needs, specifically for effector function, which involves optimal cytokine production. (Chang, et al, 2013)

Altered susceptibility to HIV-1 infection has been observed in multiple cohorts worldwide. There are individuals who are continuously exposed to HIV-1 yet remain uninfected. (Fowke, *et al*, 1996; Plummer, *et al*, 1999; Fowke, *et al*, 2000; Ball, *et al*, 2007; Young, et al, 2011) Through global whole blood gene expression analysis, energy metabolism pathways conducted in this cohort showed differential expression in HIV-1 exposed yet seronegative CSWs. (Songok, *et al*, 2012)

Methods: Study population was drawn from the Pumwani Sex Worker Cohort, Nairobi. Study groups included: HIV highly exposed yet seronegative (HESN) CSWs (>7 years); newly enrolled HIV-uninfected (<7 years); (n=6 each). Total RNA was extracted from PBMCs using Trizol (Invitrogen, USA) and cDNA synthesized. The Human Glucose Metabolism Profiler PCR array profile was used for expression of genes involved in the glycolysis, TCA and pentose phosphate pathways. qRT PCR was used to compare expression of glycolysis genes.

Results: Expression of genes in the Tricarboxylic Acid Cycle (Krebs Cycle) and Glycolysis Pathway were significantly lower in HESNs compared to the newly enrolled HIV uninfected CSWs. These are: ATP citrate lyase (ACLY) ($p<0.039$), Oxoglutarate (alphaketoglutarate) dehydrogenase lipoamide (OGDH) ($p<0.026$) and Succinate-CoA ligase-alpha (SUCLG1) ($p<0.0097$), Hexokinase-1 ($p<0.0323$), Phosphoglucose-isomerase ($p<0.0477$).

Conclusion: Significantly lower mRNA expression of ACLY, OGDH, SUCLG1, HK1 & PGMI, was observed in HESNs when compared to their uninfected yet susceptible counterparts. Enzyme expression, oxidative phosphoylation and ATP determination studies are underway to understand the role of energy metabolism in HIV resistance.

BSP3.02

Identification of endogenous retroviral protein coding sequences in the Major Histocompatibility Complex region of Cynomolgus Macaque

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The Major Histocompatibility complex (MHC) plays an important role in the immune response in primates. Although Cynomolgus macaques have become an important animal model in biomedical research, relatively little is known about the genomic structure and sequences of their MHC region. To address this issue we sequenced a segment of Cynomolgus Macaque MHC region. Complete gene structures of the genomic DNA fragment were identified using GENSCAN (http://genes.mit.edu/GENSCAN.html) that predicts the locations and exon-intron structures of genes in genomic sequences. A Blast search showed that among the Coding sequences, including MHC coding sequences, identified, a segment of genomic DNA, spanning >31,000 nucleotides region, coding for 1013 amino acid protein (including viral reverse transcriptases, integrases, and matrix protein) that shares the high homology with Gag-Pol precursor polyproteins from several endogenous retroviruses from cheetah, cat, baboon, and Xenotropic MuLV-related virus RKO. The endogenous viruses integrated into germline cells and eventually become part of the host genome over the course of evolution. Identification of a complete endogenous viral Gag-Pol precursor polyprotein within the MHC genomic region shows that the effect of endogenous viral protein on host immune response should not be ignored in vaccine and therapeutic studies with animal models.

BSP3.03

HIV-1 residues under strong functional constraint are predicted by measures of evolutionary rather than population-level genetic conservation

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Background: One strategy to overcome HIV-1 evolution/diversity in vaccine design is to identify highly mutationally constrained viral epitopes as immunogens. Population-level HIV-1 sequence conservation is commonly used as a surrogate for mutational constraint, but not all conserved HIV-1 residues incur replicative costs when mutated. We hypothesize that mutationally constrained residues may be better identified by comparing HIV-1 diversity relative to SIV orthologues ("high EvC"). In contrast, some residues that are conserved among HIV-1 population isolates but not conserved among phylogenetically-related lentiviruses ("low EvC/high PopC") may represent sites of early population-level fixation of human-driven mutations in HIV and thus may not be substantially mutationally constrained.

Methods: Mutations at a "high EvC" site in $p24^{Gag}$ (L188I/D) and "low EvC/high PopC" site in $p17^{Gag}$ (E106L) were selected based on structure information and modeling methods and engineered into an HIV-1 NL4-3 reference strain backbone. VsVg-pseudotyped HIV-1 stocks were generated in HEK-293 cells and their $p24^{Gag}$ levels assessed by ELISA. Infectivity and replication capacity of wild-type NL4.3 and mutant viruses were assessed using an established GFP-reporter T-cell assay.

Results: The "low EvC/high PopC" mutant E106L showed similar viral particle production, infectivity and viral spread to wild-type NL4-3. In contrast, the "high EvC" mutant L188D showed no evidence of viral particle production, infectivity or viral spread, suggesting a viral egress defect. Interestingly, the "high EvC" mutant L188I, where the conserved residue was replaced with a structurally similar amino acid, showed viral particle production comparable to that of NL4-3, but poor infectivity and viral spread; suggesting a viral entry defect.

Conclusions: The initial sites tested provide proof-of-concept that EvC can be used as a probe to identify virological constraint and/or potential host adaptation early in the pandemic, and to identify candidate regions for immunogenicity assessments in the context of vaccine design

BSP3.04

HIV Transmission Networks among Injection Drug Users in Pakistan

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Background: Pakistan is currently facing a concentrated HIV epidemic among injection drug users (IDUs). 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 injection drug users located in major urban centres in Pakistan.

Methods: Dried blood spots (DBS) were collected on Whatman 903 cards from IDUs in Karachi (n=300), Hyderabad (n=300) and Peshawar (n=257). Nucleic acids were extracted using an easyMAG instrument. *Protease* and part of the *reverse transcriptase* genes were amplified and sequenced using an in-house HIV genotyping assay. Transmission networks were re-constructed using publically available bioinformatics software.

Results: In total, 96 HIV *pol* sequences were generated from the 827 DBS cards. The majority of those sequences (75%) formed connected nodes arranged in 7 clusters, ranging in size from 3 to 33 individuals. Clusters were mainly homogeneous, in which 87 inferred transmission events (90.6%) occurred within a particular city. A small number (9.4%) of transmission events occurred between cities. The highest number of inter-city transmission events (7.3%) occurred between Karachi and Hyderabad while only 2 (2.1%) occurred between Karachi and Peshawar. Transmission events were not observed between Hyderabad and Peshawar.

Conclusion: The majority of sequences analyzed formed localized transmission networks partitioned according to city of collection, although some inter-city linkages are apparent. 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.

BSP3.05

Killer-cell immunoglobulin-like receptor (KIR) 3DL/DS1 and HLA class I interactions associated with HIV-1 resistance or susceptibility

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Objectives: Natural Killer cells are an important part of the innate immune response capable of targeting viral infected cells through their expression of killer cell immunoglobulin like receptors (KIR). In this study we examined the role of KIR3DL/S1 and their epistatic interactions with HLA class I genes on resistance and susceptibility to HIV-1 infection in the Pumwani sex worker cohort.

Methods: A total of 90 Resistant, 406 HIV-1 positive, and 143 HIV-1 negative women were included in this study. Exons 2 and 3 were amplified and sequenced for HLA-A, B, and C, while Exons 1-5, 7 and 9 were amplified and sequenced for 3DL1/S1. Alleles were genotyped using a taxonomy-based sequence analysis method. Associations of common 3DL1/S1 alleles and their epistatic interactions with HLA class I alleles were analyzed by using SPSS 15.0

Results: KIR3DL1*041 was independently associated with resistance to HIV-1 infection (p=0.009). Its co-existence with several class I alleles (A*74:01, p=0.049, C*06:02, p=0.013, C*08:02. p=0.034) was also associated with resistance. Several epistatic interactions with HLA class I alleles were also detected which include: 3DL1*007 with A*02:01, 3DL1*00401 with B*14:02, 3DL1*01501 with B*58:01, and 3DL1*031-B*81:01.

Conclusions: KIR3DL1 and HLA class I epistatic interactions are potential factors in resistance or susceptibility to HIV-1 infection in the Pumwani Sex-worker cohort.

BSP3.06

Blind Dating: A Phylogenetic Approach to Dating HIV Reservoir Sequences

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Background: The ability of HIV to persist within latent cellular reservoirs represents a major barrier to cure. The timing of establishment of individual viral reservoirs over the infection course may influence their susceptibility to elimination by immune-mediated or therapeutic approaches. However, methods to accurately estimate the age of reservoir sequences remain scarce. We propose a simple method to date suspected reservoir sequences using phylogenetically-informed regression.

Method: Simulated sequence data were generated using INDELible version 1.03. A total of 550 HIV RNA sequences sampled longitudinally from 11 untreated HIV-infected individuals with estimated dates of infection and a total of 3,163 HIV DNA and RNA sequences from 25 individuals were obtained from the Los Alamos National Laboratory HIV Sequence Database. The simulated and HIV RNA data were used for method validation. Maximum-likelihood phylogenies were reconstructed with RaxML. Phylogenies were rooted by determining the location of the root that minimized the root-mean-square error between root-to-tip distances and known dates of sampling. The root-to-tip distances of latent sequences were mapped to the optimal regression line to estimate reservoir establishment dates.

Results: To validate the method, we synthesized latent lineages by censoring the sample dates for random selections of up to 50% of sequences in the simulated or HIV RNA datasets. In either case, root-to-tip estimation accurately recovered these missing sample dates when the phylogeny conformed to a strict molecular clock. When this method was applied to HIV DNA sequences in phylogenies containing dated HIV RNA sequences, we observed that the predicted dates tended to precede dates of sampling, which was consistent with latency.

Conclusions: Our results indicate that the dates that HIV DNA lineages entered a latent state can be reconstructed from a phylogenetic analysis of intra-host HIV RNA sequence variation. This can provide important insights into the dynamics of HIV reservoirs within hosts.

BSP3.07

Phylogenetic clustering reveals some concordance with respondent-driven sampling recruitment chains among men who have sex with men

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Background: HIV is highly concentrated among certain groups such as men who have sex with men (MSM). The presence of sequence based transmission clusters and their relationship to respondent-driven sampling (RDS) recruitment chains based upon social-sexual networks could reveal important insights into HIV epidemic dynamics and help direct effective prevention efforts. We compared RDS recruitment chains with HIV phylogenetic transmission clusters from MSM to understand better what factors contribute to ongoing HIV transmission amongst MSM in Vancouver, Canada.

Methods: We assembled the clinical, socio-demographic characteristics, RDS recruitment chain data and viral sequence data from HIV-positive MSM recruited into the Momentum Health Study. HIV pol sequences were aligned using MAFFT v7.154b and visually inspected using AliView v1.15. Phylogenies were inferred for pol sequences from HIV-positive individuals recruited by RDS using FastTree2. Phylogenetic clusters with a tip-to-tip (patristic) distance < 0.02 were identified. Patient socio-demographic and clinical attributes were correlated with cluster membership using the R statistical framework.

Results: Of the 206 HIV-positive participants, sequences from 32 (15%) MSM grouped in 7 phylogenetic clusters. All phylogenetic clusters spanned more than 1 RDS chain (mean = 4, range = 2 - 8). In 4 clusters, individuals (n = 2 per cluster) were also members of the same RDS recruitment chain. Nearly half of the phylogenetic clusters (n = 3/7) contained individuals who HIV seroconverted during the study period.

Conclusions: We found relatively few HIV transmissions corresponding directly with the RDS recruitment chains. However, we identified 3 seroconverters in different phylogenetic clusters suggesting that RDS recruitment was successfully uncovering social-sexual networks with recent/ongoing HIV transmission.

BSP3.09

Potential effects of TILRR (FREM1 isoform 2) in HIV-1 vaginal infection through interacting with TNFa and RANTES

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Background: TILRR is a novel regulatory component, which stimulates host defense against infection through binding of IL-1R1 and TLR complex and enhancing the recruitment of MYD88 in the Ras-dependent NFKB signal transduction pathway. Our previous study has identified FREM1 as a novel candidate gene in resistance and susceptibility to HIV infection in the Pumwani Sex worker cohort. In this study, we investigated the effect of TILRR on

gene expression of several important signal transduction pathways by overexpressing it in the HeLa cells.

Methods: TILRR was overexpressed in HeLa cells using eGFP tagged plasmid construct. Transfection efficiency was determined by confocal microscopy and flow cytometry. TILRR RNA overexpression confirmed by qRT-PCR. The effect of TILRR on the expression of 252 genes in important signaling pathways was subsequently investigated by qRT-PCR with 3 PCR arrays (Human signal transduction, NFKB signaling, and MAPKinase pathways).

Results and Discussion: Overexpression of TILRR significantly upregulated 104 genes and downregulated 24 genes in these three pathways ($p<0.05$). Out of 24 downregulated genes, an important correlation observed among TILRR, TNFa and CCL5/RANTES. TILRR negatively regulated the TNFa and CCL5. Overexpression of TILRR decreased the expression of TNFa and RANTES, which might be a potential link for HIV-1 infection through the availability of CCR5. These findings are novel. Pathway studio analysis also showed the positive interaction between TNFa and CCL5/RANTES.

Conclusion: 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 NFKB and inflammatory responses. Because transendothelium migration, NFKB and inflammatory response pathways are extremely important in HIV vaginal transmission, further study the role of TILRR may identify novel targets and intervention technology against HIV-1 vaginal infection.

BSP3.10

Higher Sequence Diversity in the Vaginal Tract than in Blood at 3 Months Post Infection

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Background: In the majority of cases, HIV-1 infection is transmitted through sexual intercourse. Infection is typically initiated by a single founder virus which emerges from the genetic bottleneck, while in rarer instances multiple viruses are responsible for clinical infection found in blood. We sought to characterize the sequence diversity at early infection, between two distinct anatomical sites, namely the female reproductive tract versus systemic compartment, to better understand the selective events occurring at the earliest stages of infection.

Methods: 75 women from Uganda and Zimbabwe were recruited for this study within seven month of HIV-1 infection. We analyzed the genetic diversity by next generation sequencing of HIV-1 isolated from the female genital tract and compared it to the diversity of HIV-1 in blood of the same patients at the same time points. To date we were able to analyze 15 matched pairs of cervical swap and blood samples collected within three month (<90 days) and 6 matched pairs collected within seven month (<210 days) of infection.

Results: Genetic analysis of the C2-V3 region of HIV-1 Env revealed that early HIV-1 isolates within blood displayed a more homogeneous genotype (mean 2.6 clones, range 1-6 clones), while HIV-1 clones in the female genital tract showed statistically higher genetic diversity (mean 5.6 clones, range 6-15 clones). No differences in Env diversity were observed between HIV-1 subtypes A, C and D.

Conclusion: Our analysis of early mucosal infections in women revealed high HIV-1 diversity in the vaginal tract but few transmitted clones in the blood. Providing *in vivo* evidence for a mucosal sieve effect, leading to establishment of a homogenous systemic infection.

BSP3.11

Mining transcriptome data to train a classification model for the host resistance 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 resilence to HIV-1 infection. Previous studies have shown that specific genetic variants and expression profiles were associated with this phenotype. However, a quantitative model that discriminates HESNs from unexposed seronegative individuals using expression profiles has yet to be described. Conventional differential gene expression analysis lacks information on the weight of importance of explanatory variables. In this study, statistical classification (also known as machine learning), is employed to determine feature importance for model generation.

Methods: A panel of supervised machine learning algorithms from the scikit-learn library were used to train models to discriminate between HESN and non-exposed seronegative individuals. The exploratory analysis was conducted on a published dataset consisting of whole blood gene expression profiles (affymetrix HG U133) derived from 43 HESN commercial sex workers and 43 low risk controls.

Results: Many algorithms yielded models that had a mean classification accuracy > 80% including Random Forests, Extra Trees, Stochastic Gradient Descent, and support vector machines by cross-validation (leave-one-out, stratified shuffle split and 10 K-fold). Here, we compared and visualized the tendency of groups and specific individuals

to be misclassified in generated cross-validation models. Furthermore, we described the features selected and the variable importance of models trained from the entirety of the dataset, using configurations that yielded the best distribution of cross-validation models in terms of classification accuracy.

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

BSP3.12

The Effects of Sex Hormones on Intravaginal HIV Infection in a Humanized Mouse Model

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Despite various clinical and epidemiological studies showing a correlation between hormonal status of women and their susceptibility to HIV, this area of research remains challenging to investigate experimentally. More recently, humanized mice (hu-mice), where an immunocompromised mouse is reconstituted with a human immune system, has become an important pre-clinical tool for HIV studies. In the present study, we used the NOD-RAG2$^{-/-}$ yc$^{-/-}$ humanized mouse model to study the differences in intravaginal (IVAG) HIV infection under various hormonal conditions. Hu-mice were infected IVAG at different stages of the reproductive cycle, or following Depo-Provera (a hormonal contraceptive) injection, with 10^5 -10^7 infectious units/mL of NL4.3 Bal-Env virus. Mice infected during the diestrus (progesterone-high) stage and after Depo-Provera treatment had high plasma viral loads ($6.3x10^4 \pm 8.8x10^3$ RNA copies/mL and $9.4x10^4 \pm 2.3x10^4$ RNA copies/mL respectively) at three weeks post-infection, while mice infected during the estrus (estradiol high) stage had no detectable plasma load. Mice infected during diestrus stage had lower infection rate (18/28, 64.3%), when compared to mice treated with Depo-Provera (25/30, 83.3%). However, preliminary analysis showed mice infected during diestrus stage had higher viral load in both plasma ($7.5x10^4 \pm 5.4x10^4$ vs. $1.9x10^4 \pm 1.5x10^4$ RNA copies/mL; $p>0.05$) and vaginal wash ($2.04x10^6 \pm 9.6x10^5$ vs. $4.9x10^5 \pm 2.4x10^5$ RNA copies/mL; $p<0.05$) compared to Depo-Provera treated mice. Interestingly, under all hormonal conditions, viral load was highest in vaginal tract at week 1 and decreased over time (5-12 weeks), while plasma viral loads increased over time post-infection. Human cell reconstitution in the blood and different doses of IVAG HIV inoculation did not have any effect on plasma viral load detected in Hu-mice infected at diestrus stage or following Depo-Provera treatment, 5 weeks post inoculation. In summary, these results show that reproductive hormones play a critical role in intravaginal HIV infection and viral replication.

BSP3.13

Mutations in HIV-1 Nef associated with distinct disease outcome and their compensatory mutations

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Background: Compensatory mutations in HIV-1 restore the function of viral proteins that are compromised by escape mutations under selective pressure. They can have an impact on viral fitness and disease progression. Here we investigated mutations in Nef correlated with differential disease outcome and the impact of compensatory mutations on rates of CD4 decline.

Methods: 326 subtype A1 Nef sequences from treatment-naïve patients from a Kenyan sex-worker cohort were generated using 454 pyrosequencing. Positively selected (PS) mutations were determined using quasi analysis. Compensatory mutations were identified using phylogenetically-corrected odds ratio (PhyloDOR) predictions that compare and measure the strength of selection pressure on viral sequences by HLA alleles.

Results: We previously identified 5 mutations in Nef associated with different disease outcomes: E70D, I109V and I176M were associated with rapid CD4 decline (p=0.010, 0.015, 0.025 respectively); H124N and K190M were associated with slower CD4 decline (p=0.001 and p=0.029). Of these, amino acids (K, M, or R) at position 190 show the highest number of compensation events for escape mutations in Nef; they co-exist with substitutions at 17 different locations. Using Kaplan-Meier survival analysis we compared the rate of disease progression in patients when an escape mutation co-existed with a different amino acid at 190. The results showed that when a replacement mutation is paired with a mutation at residue 190, the rate of CD4 decline is faster than when the two amino acids occurred separately. The occurrence of I109-M190 significantly increased CD4 decline (p=0.015). The other compensatory mutations only showed a trend in faster disease progression; these are I109-K190, Q192-K190, and M176-R190.

Conclusion: The high number of compensatory events at Nef 190 indicates that this residue plays a crucial role in maintaining the function of Nef. Identifying escape mutations and compensatory mutations and correlating them with disease outcome can better inform therapeutic strategies.

BSP3.14

Increased Copy Number of Interferon-Stimulated Response Element (ISRE) in HIV-1 Long Terminal Repeat (LTR) is Associated with Hastened HIV Disease Progression

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Background: The HIV-1 LTR regulates the expression of viral genes, and hence, HIV replication. Interferon regulatory factors (IRF-1, IRF-8) have been shown to regulate the transactivation and repression of the HIV-1 LTR, via binding to the ISRE and forming a complex with NF-kB. This study examined the hypothesis that mutation(s) at the NF-kB and/or ISRE of the HIV-1 LTR may impact HIV fitness and hence, the pathogenesis observed in HIV-infected patients.

Methods: HIV-1 sequences of 5' LTR from published HIV database (n=411, Los Alamos National Laboratory) and 97 HIV-infected patients of Kenyan Pumwani Sex-Worker Cohort were analyzed using ClustalW. Longitudinal CD4 counts of antiretroviral-treatment-naïve patients enrolled in the study were used as a measure of disease progression.

Results: In all HIV-1 sequences analyzed, the LTR NF-kB binding motif was highly conserved and essentially identical in all samples, including subtypes A, A1, B, C, and D. Similarly, the LTR ISRE motif was also highly conserved, with >99% identity. However, some LTR sequences contained two-tandem ISRE motifs. The majority of these 2-ISRE sequences were found in subtypes A1, A1-recombinants, G, and U. Longitudinal study of HIV provirus from HIV-infected patients (n=6) showed conservation of LTR sequences over time (4-9 years). When HIV-infected patients were grouped into 1-ISRE and 2-ISRE, based on HIV-1 provirus sequences, the 2-ISRE patients had a relatively faster drop in CD4 counts, suggesting a more rapid disease progression.

Implication: The NF-kB motif and ISRE of HIV-1 LTR is likely highly critical to viral fitness, as the sequences are conserved over time and between different subtypes examined. Furthermore, duplication of ISRE in the HIV-1 LTR may contribute to increased viral replication and hasten disease progression.

BSP3.15

Using CD4-aptamer-siRNA chimera to mimic the modestly reduced IRF-1 expression observed in HIV-exposed sero-negative (HESN) Kenyan female sex workers

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Background: Interferon regulatory factor-1 (IRF-1) plays an essential role in mediating both the anti-viral interferon response and the early trans-activation of HIV-1 promoter. Modest reduction in IRF-1 expression was observed in Kenyan HESN female sex workers. Furthermore, in-vitro knockdown of IRF-1 expression in peripheral blood cells using siRNA to the level observed in HESN women significantly reduced the trans-activation of HIV-1 genes and hence, hampered HIV-replication. This study examined the knockdown of IRF-1 in cervical mononuclear cells (CMC) using siRNA, and tested the delivery of IRF-1 specific siRNA using CD4-binding aptamer chimera (CD4-AsiCs) into the vaginal vault of humanized BLT mice.

Methods: CMC from consented healthy donors who underwent routine pap-smear test were obtained from cyto-brush. CMC were transfected with IRF-1 specific or a scrambled control siRNA using Nucleofection technology. CD4-AsiCs specific for IRF-1 were synthesized using reverse-transcription and RNAase-resistant dNTP. CD4-AsiCs (8 pmol) in 0.5% HEC gel was administered vaginally into Humanized BLT mice on day-0 and day-1. Vaginal tissue and immune organs were harvested on day-3. Cell suspension was then prepared for flow cytometry. siRNA was labeled with Cy3, for visualization.

Results: IRF-1 expression in all CMC could be successfully reduced using siRNA by Nucleofection, and in CD4+ CMC using IRF-1 specific CD4-AsiCs (in culture). When administered into humanized BLT mice (n=1), IRF-1-specific CD4-AsiCs were taken up by cervical cells, including epithelial cells. CD4-AsiC+ cells were also found in human CD45+ cells in submandibular lymph node, spleen and rectal tissue. These hCD45+CD4-AsiC+ cells exhibit notable knockdown in IRF-1 expression, as assessed with flow cytometry.

Summary: Vaginal delivery of functional IRF-1-specific siRNA using CD4-AsiCs was efficient in knocking down modest level of IRF-1 expression systematically. However, this finding requires further validation, and the impacts of IRF-1 knockdown in-vivo on immune regulation and cellular susceptibility to infection would require further study.

BSP3.16

Comparison of two methodologies for an Illumina MiSeq-based HIV drug resistance assay

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Background: Conventional Sanger sequencing (SS)-based HIV DR assays are insufficient to reliably detect low abundance DR variants (LADRVs). With high data throughput and proven accountability for detection of LADRVs, next generation sequencing (NGS) technologies are emerging as the preferred method for HIV DR testing. Here we present and compare two Illumina MiSeq-based HIV DR testing methodologies; Nextera approach (protocol 1) and amplicon approach (protocol 2), for their performance in batched HIV DR analysis.

Methods: To minimize variability introduced by RNA extraction and RT-PCR, the same first round PCR amplicon generated for SS (covering all DR sites in HIV-1 protease and reverse transcriptase genes) was used for both MiSeq-based protocols. For protocol 1, shot-gun libraries were prepared from a single nested-PCR amplicon, following the Nextera® XT Sample Preparation kit. For protocol 2, nested-PCR was performed with adaptor-ligated primers to generate 2 overlapping amplicons (each ~500bp), followed by a limited-cycle PCR to construct uniquely-indexed amplicon libraries. Both protocols used the MiSeq v3 kit for sequencing. HyDRA, a proprietary HIV DR analysis pipeline was used for processing MiSeq derived data.

Results: The two approaches performed equally well on all examined HIV-1 subtypes with comparable error rates and sensitivity for LADRVs at >1%. All HIV DR mutations identified by SS were detected at comparable frequencies in the 2 MiSeq-based protocols.

Conclusions: Both protocols are suitable alternatives to SS-based methods for genotypic HIV DR testing. Our amplicon approach to library preparation for MiSeq-based sequencing offers the same enhanced sensitivity, accuracy, and precision as the Nextera-based approach, while simultaneously providing a 40% reduction in cost per sample as compared to SS. This method can also be effectively scaled up and automated to allow for up to 384 specimens to be sequenced in a single MiSeq run.

BSP3.17

Fine Mapping of the 9p22.3 Locus Implicates a Novel Microsatellite with the HIV-Exposed Seronegative Phenotype

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Background: We previously reported a genome-wide association study of women in the Pumwani commercial sex worker cohort wherein the minor allele of an intronic SNP rs1552896 (NM_144966.5: c.1881+58G>C), in the gene FRAS1 related extracellular matrix 1 (*FREM1*, MIM: 608944), was shown to be significantly enriched in HIV-exposed seronegative (HESN) individuals. The present study further investigates the potential role of additional *FREM1* variants in HIV acquisition risk.

Methods: We performed full-length pyrosequencing (n=69) of *FREM1* to identify variants and establish the underlying linkage disequilibrium (LD) structure of this gene. Fine mapping for HESN cases (n=113) and HIV positive controls (n=1245) was conducted at potentially causal loci, which were identified via annotation with SIFT, PolyPhen-2, and RegulomeDB/ENCODE. Significant associations, and their effect sizes, were identified with SPSS 22.0, and adjusted with Bonferroni correction.

Results: Through pyrosequencing, we discovered a novel microsatellite (specifically, a complex tandem tetranucluotide repeat) which fine mapping revealed to be hypervariable ($(CCCT)_{(1\text{-}10)}(TCCT)_{(5\text{-}20)}$), with 81 size homoplasious alleles identified. Of these, "mi8*7" ($(CCCT)_8(TCCT)_7$) associated with HESN ($p=7.50 \times 10^{-3}$, OR=2.17, 95% CI 1.21-3.88; p=0.0225 adjusted). This represents a slightly stronger association with HESN compared to rs1552896 ($p=8.77 \times 10^{-3}$, OR=2.15, 95% CI 1.20-3.84, $p=0.0260$ adjusted), to which mi8*7 is in LD (LOD 84.9, D' 0.592, r^2 0.348). Further analysis showed that homozygosity for shorter repeats (44-68bp) associated with HESN ($p=1.99 \times 10^{-4}$, OR=2.22, 95% CI 1.45-3.40, $p=5.97 \times 10^{-4}$ adjusted) when compared to genotypes with longer repeats (72-104bp). Annotation with RegulomeDB shows this locus to be a binding site of transcription factors (POLR2A, EWSR1, and FLI1) which may support the notion that we have identified causal variants.

Conclusion: To our knowledge, these results are the first to suggest the involvement of a hypervariable microsatellite with HIV acquisition phenotypes.

HIV Prevention (Preclinical), Including Antiretrovirals, Microbicides, Vaccines, and HIV Resistance
Prévention (préclinique) du VIH, antirétroviraux, microbicides, vaccins et résistance au VIH compris

BSP4.01

Differential Efficacy of Antiretroviral Drugs in Different Cellular Reservoirs

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Background: Microglia and perivascular macrophages are productively infected by HIV-1 forming the principal viral reservoir in the brain. The relative susceptibility of this viral reservoir to antiretroviral therapy (ART) is unknown. We investigated efficacy in HIV-infected myloid cells, *in vitro* extracellular and intracellular, and *in vivo* concentrations of ART.

Methods: Human microglia (HFMs), bone marrow derived macrophages (BMDMs) and PBMCs were infected with HIV-1_{YU-2} at a multiplicity of infection (MOI) 0.1-1.0. HIV-infected cells were treated with zidovudine (AZT), etravirine (ETR), raltegravir (RAL), darunavir (DRV) or maraviroc (MRV). The EC_{50} levels were determined at day 4 or 5 post-infection by p24 ELISA. HPLC MS was used to acertained the extracellular and intracellular concentrations of ART in differentiated human THP-1 cells, and in mice.

Results: Treatment of HIV-1 infected HFMs and BMDMs revealed the following EC_{50} levels at day 5 post-infection of HFMs: AZT (93.2 nM), RAL (7.4 nM), MVC (1.9 nM), DRV (22.2 nM), and ETR (12.1 nM). AZT and RAL EC_{50} levels in BMDMs were 63.9 nM and 50.4 nM, respectively. The EC_{50} levels for AZT, RAL, ETR and MVC in PBMCs at day 4 post-infection were: 7.4 nM, 2.7 nM, 2.7 nM and 6.3 nM respectively. Exposure of RAL (44.4ng/ml) and DRV (100ng/ml) to differentiated THP1 cells showed that the extracellular concentrations were 65.95 ng/ml and 90 ng/ml respectively, while the intracellular concentrations were 1.2 ng/ml and 2.4 ng/ml, respectively. *In vivo* concentration of DRV in mice was 25 fold lower in the brain compared to the peripheral circulation at 1hr postinjection.

Conclusions: EC_{50} values for AZT, ETR and DRV in HIV-infected HFMs were exhibited substantially higher than those observed in PBMCs. Intracellular:extracellular concentration ratios were low for RAL and DRV. These results underscore consideration of assessing ART concentrations in different viral reservoirs in efforts to eradicate HIV-1.

BSP4.02

Regulation of Mucosal and Systemic Immune Activation and Inflammation During the Menstrual Cycle of Female Sex Workers from Nairobi, Kenya

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Background: Sex hormones modulate immune responses in the female genital tract (FGT) to allow for reproductive function. However, the impact of hormone-induced activation and inflammation on HIV susceptibility and chronic HIV infection remain elusive. In this study, we characterized cervical and circulating CD4 and CD8 T cells, circulating regulatory T cells and cervical and plasma inflammatory profiles during the follicular and luteal phases of the menstrual cycle among female sex workers (FSW) who were not using any form of hormonal contraception.

Methods: The study groups were FSW from the Pumwani cohort, Kenya, chronically infected by HIV (n=7), new to sex work (HIV susceptible:<3 years)(n=22) and HIV-exposed seronegative (HESN >7 years) (n=17). Menstrual cycle phases were characterized using days since last menstrual period and confirmed with plasma concentrations of progesterone (Luteal:Follicular ratio >2). Blood and cervical cytobrushes were collected and cells characterized by flow cytometry. Nineteen inflammatory mediators were measured in the plasma and cervicovaginal lavages.

Results: We observed a compartmentalized alteration of pro-inflammatory cytokines with a reduction in the frequency of activated $CD4^+CD69^+$ T cells in the cervix during the luteal phase (P=0.067). In the blood compartment, the luteal phase correlated with a reduced frequency of regulatory T cells (Treg; $CD4^+FOXP3^+CD25^{hi}CD127^{lo}$) (P=0.025). Concentrations of progesterone and oestratiol during the luteal phase negatively correlated with several cervical inflammatory factors. The circulating Treg count also negatively correlated with progesterone concentration during the follicular phase and migratory capacity (b7) during the luteal phase. Hormone concentrations or hormonally-induced immune alteration were similar between study groups.

Conclusion: These results support a hormonally-induced local dampening of immune activation during the luteal phase. This state of immune suppression may reduce opportunities for HIV infection but open a window of vulnerability for other sexually transmitted infections.

BSP4.03

Sexual Activity Induced Differential Alterations in T cell Activation in HIV-Susceptible and Naturally Protected Female Sex Workers from Nairobi, Kenya

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Background: Sex induces inflammation and T cell recruitment in the female genital tract (FGT), which are conditions conducive for HIV acquisition. We have suggested that in the Pumwani Sex Worker Cohort in Nairobi, a subset (5-15%) are HIV-exposed seronegative (HESN) female sex workers (FSW) who are naturally protected against HIV through reduced cervical inflammation and T cell activation. This quiescent immune phenotype correlates with duration in sex work but the direct impact of sexual activity on immune quiescence has never been formally addressed. We hypothesized that HESN women are better able to limit sex-induced mucosal immune activation/inflammation than susceptible controls.

Methods: We compared cervical and plasma inflammation (15 markers) and T cell activation (5 markers) between 33 highly exposed HESN and 36 HIV-uninfected non-HESN FSWs from the Pumwani Cohort. Participants were followed for 3 months, the first active in sex work, second month abstaining from sex work and third month resuming sex work. Enrolment and sample collection were synchronized with the menstrual cycle. Sexual activity was monitored by detecting prostate-specific antigen (PSA) in the FGT and through a behavioural questionnaire.

Results: Patterns of inflammation were different between non-HESN and HESN FSWs, but not influenced by sexual status (active, interruption, resumption) or exposure (number of clients, condom use, PSA, regular partner). HESN had lower cervical and higher plasma inflammation. In non-HESN FSWs, the mean frequency of activated CD4 and CD8 T cells and HIV targets ($CD4^+CD69^+CCR5^+$) in the FGT were influenced by sexual exposure and inflammation. In HESN, there was a significant effect of sexual exposure on the mean expression of activation markers in plasma. The regulatory T cells levels were also influenced by sexual activity in both groups.

Conclusions: This study demonstrates significant effects of sexual activity on the mucosal immune environment which may have implications for HIV acquisition risk.

BSP4.04

Hydroxychloroquine-loaded Implantable Device Suppresses Nonoxynol-9 Induced Inflammation and T-cell Activation in a Rabbit Vaginal Mucosal Model

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Background: Early recruitment of immune cells, immune activation, and elevated inflammatory status of the vaginal mucosa can increase the susceptibility of the female genital tract (FGT) to HIV infection. Therefore, decreasing T cell activation at the FGT could help preventing HIV infection. We developed a novel trackable intravaginal implant for the delivery of the anti-inflammatory drug hydroxychloroquine (HCQ). Nonoxynol-9 (N9) was used as a model of induced-inflammation and the HCQ implant system was used to assess the effectiveness in suppressing inflammation and T-cell activation in a rabbit vaginal mucosal model.

Methods: Reservoir-based polyurethane devices were fabricated via hot-melt injection molding, embedded with a radio-frequency identification (RFID) micro-transponder. The transponder can be tracked real-time by a RFID reader. The device containing HCQ (60 mg) was non-invasively implanted in the vaginal tract of New Zealand White rabbits for 6 days and challenged with 1 mL 4% N9 gel for 24 hours. HCQ levels and inflammatory cytokine production in cervicovaginal lavage (CVL) was quantitated using HPLC and sandwich ELISA. Levels of RLA-DR from isolated vaginal mucosal T-cells was investigated by flow cytometry.

Results: X-ray analysis showed the implant remaining within the rabbit vaginal tract for over 40 days. HCQ exhibited a near zero-order release profile with an average rate of 10.67 μg/mL per day. The mean fluorescent intensities of RLA-DR on isolated vaginal CD4+ and CD8+ T lymphocytes in N9-challenged HCQ pre-treated rabbits were restored to basal levels similar to the naïve group. Lower amounts of immune cell recruitment were observed in HCQ pre-treated rabbits with decreased levels of IL-1β and IL-8 in CVL.

Conclusions: We designed a novel non-invasive implantable device for delivering HCQ in rabbits intravaginally capable of suppressing N9-induced inflammation and T-cell activation. This non-cytotoxic system may be suitable for the evaluation of other drug candidates for sexually transmitted infections.

BSP4.05

Protection from vaginal infection with HIV-1 and HSV-2 using a recombinant C. crescentus based microbicide

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The HIV/AIDS pandemic is one of the largest global health concerns. The majority of new HIV-1 infections occur through sexual transmission. Several factors can increase the risk of HIV-1 acquisition including infection with Herpes Simplex Virus 2 (HSV-2), the major cause of genital herpes. HSV-2 increases the risk of HIV-1 acquisition 2-4 fold by creating breaches in the genital epithelium and recruiting HIV-1 target cells to the vaginal mucosa, making it a major co-morbidity for HIV-1 acquisition. As there is no highly effective method to prevent both HSV-2 or HIV-1 infection, a dual-target prevention option could be an efficient means to halt infection with both viruses. We have previously described the generation of an HIV-1 specific microbicide using S-layer mediated display technology of the non-pathogenic, freshwater bacterium *C. crescentus*. By displaying anti-HIV proteins such as fusion inhibitors, antiviral lectins and decoy receptors in the S-layer of *C. crescentus* we have demonstrated up to 97% protection from HIV-1 infection *in vitro*. After confirming that *C. crescentus* appears safe for topical application to the vaginal tract, we performed *in vivo* testing for protection from HIV-1 infection using the humanized bone marrow-liver-thymus (BLT) mouse model. Of the fifteen different recombinant *C. crescentus* generated, 10 were able to provide greater than 40% protection from HIV-1 infection *in vivo*. Seven of these candidates were proposed to have anti-HSV-2 activity. *In vivo* testing with HSV-2 in C57Bl/6 mice indicated that 5 of these candidates were able to provide significant protection from HSV-2 infection, in addition to HIV-1. Taken together these results suggest that a *C. crescentus* based microbicide might be a safe and effective method for HIV-1 and HSV-2 prevention, which could have a major impact on global public health.

BSP4.06

Multivalent HIV-1 env-based pseudovirus vaccines elicit broad humoral immune response in human CD4 B cell transgenic mouse model

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Background: Although 20-30% of patients produce anti-HIV-1 broadly Neutralizing Antibodies (bNAbs), their elicitation through vaccination is still a mystery. Patient-derived bNAbs exhibit unusual characteristics attained through unclear mechanisms: elongated CDR3 loop, high rates of somatic hypermutations, polyreactivity and even autoreactive. Continuous diversification of HIV-1 quasispecises within individuals might play a role in germinal centers' (GC) physiological processes. Here we generated a multivlaent HIV-1 env-based pseudovirus as vaccine candidate and utilized a sequential immunization strategy to investigate the possibility of eliciting broad humoral immune response in a human CD4 B cell transgenic mouse model.

Methods: A variety of HIV-1 gp160 genes, including 25 parental HIV-1 strains and 25 intersubtype env recombinants were used to generate pseudoviruses through a yeast based/HIV-1 cloning system. The resultant pseudoviruses were used in single or in pool to immunize wild-type (WT) BALB/c and human CD4 B cell transgenic mice. The mice were repeatedly vaccinated with 5 or 25 different vaccines or sequentially vaccinated 5 times with 5 different vaccines for each vaccination. The immune sera were detected for both binding and neutralizing anti-HIV-1 antibodies.

Preliminary Results: All immunized mice were tested positive on a HIV-1 gp140 ELISA. Even though there was no significant difference in antibody titer among different groups, there was broader neutralization activity in groups receiving sequential vaccination, which demonstrated the ability of inhibiting different HIV-1 isolates, including HIV-1 isolate A91 (subtype A), ZM197M.PB7 (subtype C, tier 1B), and A1U 263-8 (recombinant, tier 2). Furthermore, the human CD4+ B cell transgenic mice were elicited stronger and broader neutralization activity than wild-type mice.

Conclusion: Our preliminary data showed that the sequential immunization with a multivalent HIV-1 vaccine might broaden antibody responses against HIV-1 in the human CD4+ B cell transgenic mouse model.

BSP4.07

Development of a Mass Spectrometry-Based Absolute Quantitation Method of Griffithsin, a Viral-Entry Inhibitor and Candidate Microbicide Against HIV

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PREVENT (Pre-exposure prevention of viral entry) is a preclinical trial with the goal of determining the efficacy of griffithsin, a potent HIV-entry inhibitor, as a rectal/vaginal microbicide. In order to study the pharmacokinetic and pharmacodynamic responses to griffithsin in biological matrices of non-human primates and humans, an accurate quantitation method of griffithsin is required. The goal of this study is to design a multiple-reaction monitoring (MRM) method for the absolute quantitation of griffith-

sin in biological samples using a triple quadrupole mass spectrometer.

Using in-silico digestion, theoretical surrogate peptides representative of griffithsin were selected for the development of an MRM assay. Griffithsin protein was digested with trypsin and prepared for mass-spectrometry analysis. Peptides were analyzed by MALDI-TOF (Bruker) for peptide selection and a triple-quadrupole (ABSciex) mass spectrometer for quantitation. MALDI-TOF data was analyzed using Mascot (v2.4, Matrix Science). Software for analysis included Analyst® (ABSciex), MultiQuantTM (ABSciex) and Skyline (ABSciex) for protocol optimization.

Theoretical surrogate peptides representative of griffithsin (peptides starting with FGPY, FGGS, VIQI) were chosen, of which two were confirmed (FGGS: m/z 1682.854; FGPY: 1712.820) by MALDI-TOF and the third below limit of detection. Peptide digests showed 42% coverage of the entire griffithsin sequence. Elution times of the griffithsin peptides were determined, where all three surrogate peptides were observed at 53.47 (FGGS), 37.06 (FGPY) and 45.93 (VIQI) minutes. Optimization of the MRM assay on the triple quadrupole is ongoing.

This study demonstrates proof-of concept of the sensitivity and accuracy of mass spectrometry to quantify griffithsin. Future studies will evaluate this method to quantify griffithsin in biologically relevant tissue and mucosal samples. This is important for the evaluation of the pharmacokinetic and pharmacodynamic responses observed in biological matrices of non-human primates and humans treated with griffithsin as a rectal/vaginal microbicide. This work was funded by NIH grant # U19 AI 113182.

BSP4.08

Development of Antibody-modified Chitosan Nanoparticles for the Targeted Delivery of siRNA Across the BBB as a Strategy for Inhibiting HIV Replication in Brain

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Human immunodeficiency virus (HIV) infection in the brain causes neurological consequences such as neuroinfections and neurological deterioration. HIV can infect brain astrocytes using CD4-independent mechanisms and remain dormant once inside. Utilizing receptor-mediated transport systems, nanocarriers can deliver adequate therapeutic doses to the brain to treat/control the progression of HIV. Chitosan (CS) is thought to be an ideal polymer because it is biocompatible, biodegradable, and has been shown to open cellular tight junctions. Here we rationalize that by coupling CS nanoparticles (NP) with transferrin receptor antibody OX26 (TfR-Ab) and antibody against a heavily expressed receptor on astrocytes such as the bradykinin b2 receptor (BDKRB2), a depot drug delivery system can be created. TfR-Ab allows the particle to penetrate the BBB through transcytosis whereas BDKRB2 allows for better selectivity and cell targeting through endocytosis. Tat is an HIV-1 regulatory protein that is required for efficient viral transcription. SART3 is a cellular gene that encodes Tip110, a protein that regulates Tat transactivation by binding to unphosphorylated RNA polymerase II. Tat can interact with cyclin T1 (subunit of the human positive transcription elongation factor P-TEFb) to activate the elongation of RNA polymerase II at the HIV-1 promoter. We hypothesize that knocking down both SART3 and hCycT1 (gene encoding cyclin T1) gene expression using siRNAs will interrupt the function of Tat, thus, reducing viral transcription and replication. We synthesized CS NPs with a size range of 200-280 nm as determined by dynamic light scattering and a zeta potential of -40.04 ± 0.16 mV. Cell uptake in U138-MG was significantly increased using Ab-conjugated NPs compared to non-conjugated NPs. Furthermore, the Ab-conjugated NPs significantly knocked down gene expression by 64.5 ± 5.7% for SART-3 and 47.3 ± 8.9% for hCycT1. Our technology platform demonstrates potential utility for the treatment of HIV infection in the central nervous system.

BSP4.09

Investigating stHIV-1 Integrase Drug Resistance Profiles

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Given the high cost of animal-based research for the study of drug resistance, there is a need for additional models and viruses in order to validate and extend findings previously obtained with either HIV or SIV. In this regard, simiantropic HIV-1 (stHIV-$1_{SCA,SVIF}$) virus, referred to as stHIV-1, with an 88% sequence homology to HIV-1, is a HIV-based chimera. By replacing the HIV-1 capsid and *vif* regions of the genome with the corresponding counterparts from simian immunodeficiency virus (SIV), stHIV-1 is capable of infecting both human and macaque cells. The active site of the integrase coding sequence of HIV-1 is conserved in stHIV-1. Thus, it is reasonable to speculate that stHIV-1 may be a suitable model for the study of integrase strand transfer inhibitors (INSTIs) drug-resistance mutations (DRMs).

Our objective was to verify/predict if stHIV-1 will have similar/same resistance pathways against INSTIs as HIV-1 and validate potential mutations in stHIV-1 through tissue culture studies. Our results show that stHIV-1 is susceptible to INSTIs with IC50s in the low nanomolar range; equivalent HIV-1 drug-resistance mutations in stHIV-1 (E92Q, G118R, E138K, Y143R, S153Y, N155H, and R263K) resemble HIV-1 resistance substitutions in regard to diminished drug efficacy and viral replication deficits associated with these substitutions. DTG has an improved resistance profile in stHIV-1, compared with first generation INSTIs. Additionally, rhesus PBMCs or human CBMCs were infected with

stHIV viruses and were serially passaged in the presence of increasing concentrations of INSTIs. Genotyping of the IN region of the stHIV-1 genome by PCR allowed for the identification of mutations selected in the presence of INSTIs. The development of a predictive animal model may help to identify impending resistance mutations and to possibly inform treatment decisions in humans.

BSP4.10

Development of an assay to differentiate de novo HIV-1 virus from a latency reversing activator vector vaccine.

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Background: During the acute phase of infection HIV will integrate into host cellular DNA, leading to the establishment of a latent reservoir. In order to rid the host of latent HIV-1, studies have suggested that the latent reservoir must be purged, or "shocked", to allow for host immune responses to effectively eradicate the virus. Studies are currently ongoing to design an activator vaccine (ACT-VEC), using autologous-derived virus that is intended to target the resting CD4 T cell reservoir and induce latency reversal. However, the autologous ACT-VEC is identical in protein sequence to reactivated HIV-1, creating difficulties in monitoring latency reversal using monoclonal antibodies and flow cytometry.

Methods: Amino acid residues 13-16 of the p17 region of NL4-3 have been mutated to alter the humoral epitope and disrupt binding of anti-HIV1 p17 antibody [32/5.8.42]. The impact of these p17 epitope mutations on viral protein production was assessed using p24 ELISA and gp120 Western blot, and the activity of reverse transcriptase was verified using RT-assay. The binding of mutated NL4-3 with anti-HIV1 p17 antibody was assessed using flow cytometry.

Results: We show that specific mutations placed within the p17 region have no impact on viral protein production or reverse transcriptase activity. Certain mutations could however, disrupt the binding of p17 antibody as determined by non-denaturing Western blot and intracellular flow cytometry.

Conclusion: The mutations found capable of disrupting anti-HIV1 p17 antibody binding will be utilized during construction of all ACT-VECs such that *de novo* virus may be distinguished from input ACT-VEC VLPs. This will allow for the quantification of latently infected cells undergoing ACT-VEC stimulated reversal.

BSP4.11

Expression of a SIVmac239 Gag-Pol Fusion Protein by Cynomolgus Macaque Cytomegalovirus for use in a SIV – Cynomolgus Macaque Vaccine Challenge Model

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Background: Cynomolgus macaques have become more attractive as a vaccine model for the study of HIV. Well-characterized populations from the island of Mauritius and attributes such as size and temperament make them ideal to work with. Reagents and molecular tools available for use in the cynomolgus macaque model currently lag behind those available for rhesus macaques, but development of this additional non-human primate model for vaccine studies will overcome some of the limitations offered by the rhesus macaque model.

Experimental Goal: To complement our earlier findings observing the species specificity of cytomegalovirus in cynomolgus macaques, and the development of cell lines specific to this macaque strain, we have now developed a tool, a bacterial artificial chromosome (BAC) to manipulate cynomolgus cytomegalovirus towards the end of developing a CMV-based SIV vaccine in this animal model of HIV. Specifically, we have constructed a SIV Gag-Pol fusion protein-based vaccine candidate through the development of a Mauritian cynomolgus macaque-derived cytomegalovirus, CyCMV Mauritius, as a stable BAC.

Results: Expression of a codon-optimized Gag-Pol fusion protein into a CyCMV Mauritius BAC was confirmed by western blot analysis. As with other large herpesvirus based-BACs, a number of unavoidable mutations were introduced into the virus through the cloning process. Illumina sequencing of the CyCMV Mauritius-derived BAC identify identified 789 polymorphisms across the 217 200bp, predominantly single nucleotide polymorphisms (SNPs). These resulted in changes to 65 genes, but primarily to non-essential or strain specific genes. Only two core genes were altered, UL102 and UL47, both with single amino acid changes. Importantly, we determined that the growth kinetics of the viral BAC mimic those of wild-type virus, demonstrating sustained viral fitness.

Conclusions: This viral kinetic and protein expression data demonstrate the feasibility of this CyCMV Mauritius BAC for use in vaccine immunogenicity studies in the SIV Cynomolgus macaque model.

BSP4.12

Development and characterization of a modified R88-Apobec3G-based anti-HIV approach

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Introduction: HIV-1 infection *in vivo* is characterized by persistent high-level viral replication associated with a rapid turnover of CD4+ T cells. Even though the progress in anti-HIV-1 chemotherapy in the past decades has been dramatic, virus drug resistance and the latently infected reservoir are the two major obstacles to effectively controlling and curing HIV-1 infection. Therefore, it is necessary to develop new therapeutic strategies specifically targeting these two obstacles.

Results and Conclusions: In this study, we have characterized the antiviral potential of R88-A3G$_{D128K}$ (R88-A3Gm) against drug-resistant strains of HIV-1 and viruses produced from latently infected cells. By using a doxycycline (Dox)-inducible lentiviral vector, we can introduce R88-A3Gm into CD4+ T cells, and these transduced T cells were shown to be resistant to the wild-type and various drug-resistant HIV-1 infections. Moreover, when the R88-A3Gm-expressing vector was transduced into the HIV latently infected ACH-2 cell line or resting human CD4$^+$ T cells, upon activation by phytohemaglutinin (PHA), the infectivity of progeny viruses from these cells were significantly interrupted. Furthermore, we have also generated an DNA/RNA-free virus like particles (VLPs) loaded with R88-A3Gm, and the preliminary data revealed that HIV replication in CD4$^+$ T cells was also inhibited in cells treated by VLP-R88-A3Gm. Altogether, these data provide evidence that R88-A3Gm-based anti-HIV gene therapy may be capable of targeting both active and latent HIV-1 infected cells to prevent subsequent viral replication and dissemination.

BSP4.14

The Presence of Natural SIV Antibodies and Inducible Endogenous SIV-like Antigens in Mauritian Cynomolgus Macaques

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Cynomolgus macaques (Macaca fascicularis) are an increasingly used non-human primate model in biomedical research including HIV vaccine development. However, natural immunity to SIV or related endogenous retroviruses in these animals, as described in this report, needs to be taken into consideration in vaccine projects, including animal selection, experimental design and result interpretation. In this study, we screened 108 female Mauritian Cynomolgus macaques for natural antibodies to SIV antigens. These antigens included 12 20mer peptides overlapping the 12 protease cleavage sites (-10/+10), respectively (PCS peptides), and 3 non-PCS Gag or Env peptides, derived from SIVmac239. The peptides are conserved among multiple SIV strains. The screening revealed various levels of natural antibodies to these SIV antigens with subsets of monkeys showing high antibody levels, although the monkeys were not infected by SIV or other known retroviruses. Interestingly, vaccination of monkeys with PCS peptides (in recombinant vesicular stomatitis virus) (rVSVpcs) also induced antibody responses to all the 3 non-PCS peptides, despite the fact that the non-PCS peptides share no sequence homology with the PCS peptides. This suggests that the rVSVpcs vaccination possibly activated dormant SIV-like endogenous retrovirus(es) that subsequently induced host immune responses to the viral antigens. Mass spectrometry and Western blot analyses of monkey plasma confirmed significant increase of SIV/HIV-like antigens and antibodies recognizing purified recombinant SIV Gag p55 and Env gp130. Our observations in Cynomolgus macaques are consistent with the recent findings in humans that HIV infection triggers the expression of some human endogenous retroviral genes. We speculate that activation of dormant SIV-like endogenous retroviral antigens in Cynomolgus macaques by external stimuli may be a potential cause of natural antibodies that recognize SIV antigens.

BSP4.15

Sequential purification of highly specific antibodies against peptides of SIV protease cleavage sites (PCS) from crude monkey plasma

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Background: Developing an effective preventative and therapeutic vaccine for HIV-1 has been the best hope to end the pandemic, although proved to be an enormous challenge. HIV protease has been a major therapeutic target. A vaccine targeting the 12 protease cleavage sites (PCS) could be effective. Using Mauritian Cynomolgus Macaques and SIVmac251 as an experimental model, 12 peptides of the SIV PCS were used to immunize monkeys simultaneously. Each monkey was screened for antibody activities against each injected peptide with Bioplex assays before and after vaccination. The crude plasma containing multiple polyclonal antibodies were collected and stored at -80o C.

Method: An immunoaffinity chromatographic technique to sequentially purify polyclonal antibodies with specificities against each of its respective 12 peptide of SIV PCSs (PCSn, n=1-12) from crude monkey plasma was developed to study the therapeutic and preventive effects of the antibodies. The technique, utilizing immobilized peptide specific to SIV PCSn onto CarboxyLink Resin, allowed purification of very low level of corresponding specific antibodies.

Results and Significance: The conditions for coupling peptide and purifying antibodies have been optimized to sequentially separate multiple antibodies against the respective SIV PCSn in the same crude plasma samples. Bioplex assays showed that this procedure generated high specific polyclonal antibodies against the SIV PCSn. Native and SDS gel analysis suggested good antibody preparation specificity in a reproducible manner. Larger amount of antibodies against each PCSn will be prepared for epitope mapping assays and also to further study the preventative and therapeutic effects. The method uses rounds of stringent washes to overcome the possible antigen and antibody cross-reactions caused by multiple antigens with low sequence complexity epitopes (PCSn of 20 amino acids).

BSP4.16

Genital – Systemic chemokine gradients and the risk of HIV acquisition in women

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Background: Mucosal and systemic immune mediators have been independently associated with HIV acquisition risk, but the relationship between compartments remains unclear.

Methods: To address this, the concentrations of 12 cytokines were compared in matched plasma and cervicovaginal lavages (CVLs) from 57 HIV positive women prior to their acquisition of HIV (cases) and 50 women who remained uninfected (controls) during the CAPRISA 004 trial.

Results: While genital IP-10 concentrations were significantly higher in cases, plasma IP-10 concentrations were inversely associated with HIV risk. Comparing differences in mucosal and systemic cytokine concentrations between cases and controls, mucosa-biased gradients indicating higher CVL relative to plasma concentrations were observed for all 5 chemokines in the panel. Four were significantly associated with HIV acquisition, including IP-10 (OR 1.73, 95% CI 1.27-2.36), MIP-1β (OR 1.72, 95% CI 1.23-2.40), IL-8 (OR 1.50, 95% CI 1.09-2.05) and MCP-1 (OR 1.36, 95% CI 1.01-1.83). None of the other 7 cytokines tested predicted HIV risk. Decision tree analyses confirmed this association, with gradients of IP-10, IL-8, and GM-CSF concentrations correctly classifying 77% of HIV outcomes.

Conclusion: Our findings suggest that mucosa-biased gradients of IP-10, MIP-1β, IL-8 and MCP-1 are associated with an increased risk of HIV infection.

BSP4.17

Dolutegravir resistance alters HIV replicative capacity

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HIV drug resistance against dolutegravir is associated with the emergence of the R263K substitution in integrase. Discrepancies in the identification of the R263K resistance substitution in different tissue culture experiments led

us to examine the replicative capacity of dolutegravir-resistant HIV-1 in various immortalized and primary human immune cells.

We performed in vitro HIV-1 infections of PM1, CEM and Jurkat immortalized T-cell lines as well as primary human dendritic cells, macrophages and primary CD4+ T-lymphocytes. Various HIV-1 drug-resistant viruses were used as controls. HIV-1 replication was monitored through measurement of reverse transcriptase activity in the culture fluids and/or HIV-1 RNA-specific reverse transcription PCR. Alu-mediated quantitative PCR was used to measure HIV-1 DNA integration.

Our results show that dolutegravir-resistance can alter HIV-1 tropism, favoring replication in some cell types and not others.

BSP4.18

Dolutegravir resistance decreases HIV-1 DNA integration

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Resistance against the integrase strand-transfer inhibitor dolutegravir can be associated with the R263K resistance substitution in HIV integrase. Previous studies have shown that R263K decreases viral replicative capacity and integration in short-term infectivity assays. Given the importance of integration in the establishment of latency, we investigated the effects of dolutegravir-resistance on HIV integration in long-term infections.

HIV-1 integration was measured by Alu-mediated QPCR over 3 weeks infection of PM1 cells with wild-type or dolutegravir-resistant R263K-containing viruses. Viruses were harvested from infected cells and then used to initiate subsequent rounds of infection. Levels of integration were normalized and expressed relative to integration of the wild-type virus after 1 week. Means ± standard deviations were calculated and the Student's t-test was used to evaluate significant differences.

The results show that dolutegravir resistance was associated with a progressive decline in the levels of integrated HIV DNA over subsequent infection cycles, beginning with an initial impairment that approximated 30%.

Substitutions that are associated with HIV-1 resistance against dolutegravir impair the long-term ability of HIV-1 to achieve integration. The feasibility of therapeutic strategies using dolutegravir to decrease the size of the HIV reservoir through the development of integration-defective viruses should be explored.

BSP4.19

Integrase Inhibitor Selection in Tissue Culture Using NRTI Mutant Viruses Favours Dolutegravir as an Effective Therapeutic Partner

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Introduction: Current HIV treatment strategies couple integrase inhibitors (INIs) with nucleoside reverse transcriptase inhibitors (NRTIs). Previously, we reported that the tissue culture selection of viruses resistant to reverse transcriptase inhibitors is impaired by the presence of mutations conferring resistance to dolutegravir (DTG). In this study, we have investigated the outcome of INI drug pressure on viruses bearing NRTI resistance mutations *in vitro*.

Methods: Cord blood mononuclear cells were infected with recombinant pNL4.3 viruses with wild type (WT), M184I, M184V or K65R site-directed mutations and selected with DTG, elvitegravir (EVG) or raltegravir (RAL). Drug concentrations were increased gradually to encourage the emergence of resistant variants. Virus growth was monitored by weekly determinations of reverse transcriptase activity. Viral RNA was extracted from tissue culture supernatants and sequenced to identify changes in the integrase region.

Results: Varying abilities to overcome increasing drug pressure were observed. The R263K mutation arose from the WT control under DTG pressure as a mixture at week 17 and was fully selected before week 22. The NRTI-resistant viruses were unable to escape DTG pressure and no mutations arose after more than 26 weeks in culture. EVG treatment was easily overcome by week 12 in all cultures. RAL showed a more variable profile, whereby RAL mutations appeared by week 12 for WT and M184V viruses, and by weeks 22-26 for M184I and K65R viruses. Reversion of the M184I/V mutants was prevented by low-level lamivudine treatment while minimal tenofovir treatment maintained the K65R substitution. In cases in which the escape of mutants was delayed, the escalation of drug concentrations was not always possible to sustain strong antiviral activity.

Conclusion: In our tissue culture model, development of resistance to DTG was appreciably hindered if NRTI-resistance mutations were present. Antiretroviral regimens pairing NRTIs with DTG may provide a superior tactic for successful treatment.

BSP4.20

Effect On Viral Fitness Of DTG-Resistance Mutations In NRTI/NNRTI Resistant Viruses

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In treatment-experienced patients treated with DTG-based regimens, the R263K substitution has been commonly found in rare cases of treatment failure. R263K is also selected in vitro under DTG pressure and can be followed by the emergence of H51Y as a secondary mutation. Viruses carrying R263K substitution alone or in combination with other major/secondary mutations in RAL/EVG pathways have a significant decrease in viral fitness, DNA integration capacity and integrase strand transfer enzymatic activity. However, little information has been reported for viruses combining RT- and IN-resistance mutations. Currently, DTG has been co-formulated with abacavir/lamuvidine or tenofovir/emtricitabine as recommended regimens for antiretroviral therapy (ARV)-naive patients and with Rilpivirine in the ongoing clinical trials SWORD-1 and SWORD-2 phase IIIb/IV in treatment-experienced patients. We previously showed that the combination of M184I/V(RT) and R263K(IN) further decreased viral fitness compared to each single mutation and no development of DTG and 3TC cross-class resistance was observed. Here we extend on our previous study with the addition of R263K or H51Y-R263K to major clinically-relevant RT substitutions K65R, L74V, K103N, E138K and M184I/V in the absence of drug pressure. These mutations commonly emerged alone or coupled, causing virological failure with regimens containing corresponding inhibitors ABC/DDI/TDF; ABC/DDI; NVP/EFV, RPV and 3TC/FTC, respectively. We found that the addition of DTG-resistance substitutions R263K or H51Y-R263K to one of these RT substitutions in the same virus caused significant reduction in viral fitness compared to single RT substitution. Double mutant R263K(IN) + RT and triple mutant H51Y-R263K(IN) + RT viruses have moderate and significant defect on viral fitness and integration capacity, respectively. Thus HIV-1 may suffer a severe evolutionary disadvantage when both resistance pathways are involved. Our findings also help to explain the virological robustness of DTG in co-administration with NNRTIs/NRTIs in HIV-1 treatment.

BSP4.21

Development of a microscopy based high-throughput HIV phenotypic resistance assay

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Background: We are developing a high throughput microscopy based HIV phenotype assay to assess HIV strains against integrase inhibitors in the Canadian population.

Method: Recombinant viruses were produced by co-transfection of patient-derived integrase gene amplicons with linearized integrase-deleted pNL4.3 plasmid into a reporter T-cell line (CEM-GXR) that produces green fluorescent protein (GFP) when infected with HIV. Recombinant viruses were harvested upon reaching 15%-40% GFP. Matching genotypes were generated for amplicons. To phenotype recombinant viruses, 1 percent of virus-infected (GFP positive) cells were plated with 10-fold dilutions of Raltegravir (RAL), Elvitegravir (EVG) or Dolutegravir (DTG) antiretroviral drugs. The 50-percent inhibitory concentrations (IC50) and fold change (FC) were determined on days 3 to 6 using the Spectramax i3 Minimax 300 Imaging Cytometer and SoftMax Pro Software for plate reading and data analysis purposes.

Results: Comparison between microscopy and flow cytometry-based assays shows concordance in fold changes across patient samples. A sample predicted to be susceptible to RAL produced FC=0.4 (microscopy based) and FC=0.7 (flow cytometry based). Repeat microscopy based testing produced FC=1.1. Similarly, a predicted RAL resistant sample produced FC= >100 with both assays. The two assays produce similar %GFP readings across samples. Additional testing and validation is underway.

Conclusion: The comparison between the microscopy and flow cytometry based methods shows that the microscopy-produced data is reproducible, matches predicted sample resistance and has equivalent %GFP sensitivity. This assay is designed to complete a single 96 well plate read in less than 5 min in order to increase throughput over conventional flow cytometry assay that takes 90 min/plate. Thus, microscopy can be used to create an accurate high throughput phenotyping assay with clinical applications.

BSP4.22

Early Expression of Lymphocyte Activation Gene-3 on Human T cells

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Rationale: Regulation of the immune system is a complex process involving many different pathways and signals. LAG-3 is an immune inhibitory marker which regulates T cell effector function when engaged. Conversely, engagement of MHC class II by LAG-3 results in activation of APCs

and recruitment of additional immune cells. Expression of immune inhibitory markers during chronic infections, such as HIV, leads to immune exhaustion. Although many exhaustion markers are up-regulated during HIV infection, LAG-3 expression is consistently low on T cells for unknown reasons. The cell subsets contributing and factors regulating LAG-3 expression are not well defined in humans.

Methods: Human PBMCs were stimulated for up to 24 hours with CD3/CD28 beads and observed by flow cytometry to determine when LAG-3 expression peaks in response to TCR engagement. T cells were also sorted into CD4+ and CD8+ subsets and stimulated with CD3/CD28 beads to asses relative contribution to LAG-3 expression. Release of soluble LAG-3 was measured by ELISA.

Results: Engagement of the TCR using CD3/CD28 beads resulted in significantly increased LAG-3 expression after 4 hours ($p = 0.0313$). LAG-3 is then down-regulated until the 16 hour time point when expression peaks ($p = 0.0313$). Consistently, the concentration of soluble LAG-3 increased significantly by 16 hours ($p < 0.05$).

A significantly greater proportion of CD8+ than CD4+ T cells expressed LAG-3 ($p = 0.0156$), 16 hours post stimulation. Conversely, CD69 expression was expressed by a significantly greater proportion of CD4+ T cells ($p = 0.0156$). These results were consistent between bulk PBMCs and sorted subsets.

Significance: The rapid expression of LAG-3 following stimulation implies an importance of this immune inhibitory marker in the early immune response. By elucidating when LAG-3 is expressed during an immune response we can better understand how and when to target this protein as a potential intervention.

BSP4.23

Expression of SIVmac239 Gag and Env Genes and Protease Cleavage Site Sequences Using the Vesicular Stomatitis Virus Vector System

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Developing an effective vaccine for HIV-1 has proved to be an enormous scientific challenge because HIV-1 targets a key component of the immune system and exhibits enormous antigenic diversity. We are conducting a pre-clinical study using Cynomolgus macaques-SIV as a model to compare the protective efficacy of two different HIV vaccines- a vaccine that generates focused immune responses to 12 protease cleavage sites (PCS) and a vaccine that generates broad immune responses to full-length GAG and ENV. To prepare for this study, we generated 14 recombinant vesicular stomatitis viruses (rVSV), each expressing a specific immunogen.

These immunogens include full-length ENV, GAG and 12, 20-amino acid peptides overlapping the PCS of SIVmac239. Nucleotide sequences of each immunogen were inserted into a modified VSV vector (Indiana strain) by restriction cloning. Each rVSV was transfected into VeroE6 and 293T using Lipofectamine 2000 and rescued. Rescued rVSV was then grown on VeroE6 cells, purified using 20% sucrose cushion gradient and quantified by $TCID_{50}$ and plaque assay. To confirm if each rVSV can express the immunogen of interest, rVSV-infected cell lysates were obtained and analyzed with reverse-transcription PCR, sequencing, indirect enzyme-linked immunosorbent assay and/or western blotting. To evaluate the immunogenicity of each rVSV in mice, BALB/c mice were vaccinated ($1x10^5$ PFU) in five groups- rVSV1-12; rVSV-ENV; rVSV-GAG; rVSV-WT and PBS. Antibody responses were monitored using the Bio-Plex multiplex system (Bio-Rad) while T-cell responses were monitored using enzyme-linked immunosorbent assay.

All 14 rVSVs (rVSV-ENV, rVSV-GAG, rVSV1-12) were able to express the immunogen of interest *in vitro* and *in vivo.* Stock rVSVs with titres of 10^{7-9} PFU/mL were obtained. Future studies involve comparing the protective efficacy between rVSV-PCS1-12 and rVSV-GAG/rVSV-ENV in a macaque model with repeat low-dose vaginal SIVmac251 challenges.

BSP4.24

Impact of Hydroxychloroquine-Loaded Polyurethane Intravaginal Rings on Lactobacilli

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Rationale: The female genital tract (FGT) is the primary site for drug delivery particularly for the treatment and prevention of sexually transmitted infections. Unfortunately, majority of microbicides when applied topically vaginally, may be cytotoxic to the normal flora within the FGT. Decrease in lactobacilli within the FGT can alter the microenvironment resulting in an increased risk of infections including HIV. Our study aims to evaluate the impact of a reservoir-type intravaginal ring (IVR) loaded with hydroxychloroquine (HCQ) on *Lactobacillus crispatus* and *jensenii,* which are the main bacteria found in the FGT.

Methods: A reservoir-type IVR was made from medical grade polyurethane using a hot-melt injection molder and loaded with HCQ and a rate controlling excipient. The *in vitro* release study was performed in 25 mM sodium acetate buffer (pH4) and in MRS broth (pH6.2). Daily HCQ release was analyzed using HPLC. The impact of HCQ alone, drug-free IVRs, and HCQ-loaded IVRs were evaluated on lactobacilli, vaginal (Vk2/E6E7) and ectocervical (Ect1/E6E7) epithelial cells, and immune cells (Sup-T1). Changes

to the integrity of the vaginal epithelial cell monolayer were also assessed.

Results: The IVR segments were capable of providing controlled release of HCQ for 24 days, with mean daily release rates of 17.01±3.6 mg/mL in sodium acetate buffer (pH 4) and 29.45±4.84 mg/mL in MRS broth (pH 6.2). Drug-free IVRs and the released HCQ had no significant effects on bacterial growth or the viability of vaginal or ectocervical epithelial cells. Furthermore, there was no significant impact on the integrity of vaginal epithelial cell monolayers, in comparison with controls, as measured by transepithelial electrical resistance.

BSP4.25

Combination Nanomicrobicide for the Efficient Gene Knockdown of CCR5 and Nef in CD4+ Immune Cells

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Introduction: This study is to develop a RNA interference (RNAi)-based nanomicrobicide for the combination delivery of small interfering RNAs (siRNAs) to knock down the host gene CCR5 and the viral gene nef as a pre-exposure prophylaxis to prevent intravaginal transmission of HIV-1.

Methods: Nanoparticles (NPs) containing siRNA targeting CCR5 and nef were prepared by a double-emulsion evaporation method with poly(lactic-co-glycolic acid)-polyethylene glycol and formulated into a hydroxyethyl cellulose gel.

Results: NPs showed a particle size of 256.6±8.3nm with a zeta-potential of -9.78±1.03mV at pH5.0 and a particle size of 246.3±10.2nm with a zeta-potential of -24.95±5.55mV at pH7.4. Encapsulation efficiency was 86.76±0.14%. NPs showed a pH-dependent release profile, with sustained release of siRNA under pH 7.4 (40% over 13 days) and minimal release of siRNA under pH 5.0 (< 5% over 48 hr). siRNA-NPs were rapidly taken up by CD4+ Sup-T1 cells (40% uptake in 2 hr; 100% uptake in 24 hr). siRNA-NPs were formulated into a vaginal gel with 17% of siRNA-NPs released within 24 hr. In a vaginal mucosal co-culture model (vaginal epithelial cells co-cultured with nef transfected CD4+ T cells), vaginal gel loaded with siRNA-NPs could efficiently knock down CCR5 (>50% knockdown) and nef (>70% knockdown) in CD4+ cells over 3 days after a 24 hr treatment.

Conclusions: We have developed a novel RNAi-based combination nanomicrobicide that can efficiently knock down CCR5 and nef in CD4+ immune cells with desirable particle size, zeta potential and pH-dependent release profile for intravaginal delivery. Formulating the nanomicobicide as a gel provides ease in administration and retention within the vagina.

BSP4.26

Drug selection facilitates phenotypic examination of integrase inhibitor resistance in a HIV variant mixture

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Background: HIV from patients can contain mixtures of virus variants in which wild-type variants outcompete drug resistant variants *in vitro*, especially in patients with recently emerging resistance. This study describes a method to produce and phenotype a recombinant virus population containing all resistant variants from a single patient virus sample with our in-house phenotype assay.

Method: Recombinant viruses were made by co-electroporation of GXR-CEM T cells with an integrase-deleted pNL4-3 plasmid and integrase PCR amplicons of a virus derived from a patient with emergent resistance to elvitegravir(EVG) The virus culture was split on the day of co-transfection and grown in the presence of raltegravir(RAL), EVG or dolutegravir(DTG) in concentrations that were 0.5 times(0.5x), 2 times(2x) and 10 times(10x) the approximate IC50. Samples of cultures were sequenced at various times and phenotyped at 34 days.

Results: The virus cultures reached at least 10% infection except when grown with DTG under 2x and 10x IC50 conditions. Sequencing of the viruses grown with 2x IC50 of RAL and with EVG showed 100% concordance with the original patient integrase sequence while other cultures lost resistance mutations over time. Phenotyping of the viruses showed high levels of EVG resistance (>100 fold change from susceptible control virus) and potential resistance to RAL and DTG (see table).

Conclusion: Growing the recombinant viruses after transfection in the drug that was part of the patient's therapy results in viruses with the greatest concordance to original patient virus sequence. Phenotypic integrase inhibitor resistance can be detected in these concordant viruses.

Fold-change (FC) response to drug relative to susceptible control

Virus grown under drug pressure	raltegravir FC	elvitegravir FC	dolutegravir FC
raltegravir (2X IC50)	27	>100	3.4
elvitegravir (0.5X IC50)	5.5	>100	2.1
elvitegravir (2X IC50)	4.7	>100	1.2
elvitegravir (10X IC50)	46	>100	3.7

HIV Virology/Pathogenesis, Including Antiviral Mechanisms
Virologie/pathogénèse du VIH, mécanismes antiviraux compris

BSP5.01

A Highly-Conserved Residue of the HIV-1-gp120 Inner Domain is Important for ADCC Responses Mediated by Anti-Cluster A Antibodies

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Human Immunodeficiency Virus 1 (HIV-1) infection elicits a potent B cell response resulting in the production of antibodies against the envelope glycoproteins (Env) which are exposed at the surface of viral particles and infected cells. We recently reported that these antibodies have the potential to eliminate HIV-1-infected cells by mediating antibody-dependent cellular cytotoxicity (ADCC). We found that these non-neutralizing CD4-induced (CD4i) ADCC-mediating antibodies are present in sera, breast milk and cervicovaginal lavages of HIV-1-infected individuals and preferentially target Env in its CD4-bound "open" conformation. However, in order to evade ADCC responses HIV-1 developed a highly-sophisticated strategy to keep Env at the surface of infected cells in the unbound "closed" conformation. HIV-1 accomplishes this through its accessory proteins Nef and Vpu, which decrease the overall amount of Env (via Vpu-mediated BST-2 downregulation) and CD4 at the cell surface. In agreement with the necessity for HIV-1 to avoid exposing Env in the CD4-bound conformation, we recently showed that forcing Env to adopt this conformation with small CD4-mimetics (CD4mc) sensitizes HIV-1-infected cells to ADCC mediated by sera, breast-milk and cervicovaginal fluids from HIV-1-infected subjects. Here, we show that a highly conserved tryptophan at position 69 of the gp120 inner domain is important for ADCC mediated by anti-cluster-A antibodies and sera from HIV-1-infected individuals. Our results confirm that Nef and Vpu protect HIV-1-infected cells from ADCC but also show that recognition of infected cells by an antibody does not necessarily translate into ADCC. This raises the intriguing possibility that the angle of approach of a given class of antibodies could impact its capacity to mediate ADCC.

BSP5.02

Nef Protein from HIV-1 elite controllers are inefficient at preventing ADCC

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Background: HIV-1 Nef is a major determinant of HIV-1 pathogenesis. Impairment of Nef function has been described in elite controllers (EC), rare HIV-1 infected individuals who suppress plasma viremia to <50 RNA copies/mL in the absence of antiretroviral treatment. Understanding viral and host elements that result in the controller phenotype may help to direct the development of new therapeutic approaches and strategies aimed at attaining a functional cure. Several studies have shown a correlation between antibody-dependent cell mediated cytotoxicity (ADCC) and disease progression. It was recently reported that elimination of HIV-1 infected cells by ADCC requires the presence of envelope glycoproteins (Env) in the CD4-bound conformation at the surface of infected cells. Interestingly, Nef clones isolated from EC are less efficient at downregulating CD4. This raises the possibility that accumulating CD4 could interact with Env at the cell surface and thereby sensitize HIV-1-infected cells from EC to ADCC.

Methods: We evaluated the ability of CD4-induced antibodies and sera from HIV-1-infected individuals to detect and mediate ADCC on primary CD4+ T cells infected with isogenic HIV-1 viruses that expressed nef clones isolated from chronic progressors or elite controllers using a FACS-based ADCC assay.

Results: Nef clones from EC were unable to fully downregulate CD4. We observed a significant increase in the exposure of HIV-1 Env epitopes targeted by ADCC-mediating antibodies at the surface of cells expressing Nef isolates from EC that correlated with their enhanced susceptibility to ADCC.

Conclusion: Our results highlight the importance of Nef-mediated CD4 downregulation in preventing the elimination of HIV-1-infected cells by ADCC. The inability of Nef alleles from EC to fully downregulate CD4 enhances the sensitivity of virus-infected cells to ADCC, which may contribute to suppression of viremia.

BSP5.03

Activation of HIV-1 Gene Expression in Latently Infected PBMCs by a Small Molecule PKC-412

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HIV-1 latency is a main obstacle in HIV-1 eradication. Extensive efforts are being directed toward the reactivation of latent HIV reservoirs with the hope that latently infected cells will be eliminated by the host immune system and/or virus-mediated cell lysis.

Methods and Results: Through virtual screening, we have identified midostaurin (PKC412), a small-molecule multiple tyrosine kinase inhibitor, which is able to reactivate viral transcription and expression from a HIV-1 latently infected ACH2 cell line and primary resting PBMCs. The cytotoxicity of PKC412 in both quiescent ACH2 cells and human resting Peripheral blood mononuclear cells (PBMCs) was significantly lower. PKC412 can reactivate HIV-1 expression in ACH2 cells in a dose and time dependent manner. Significantly, PKC412 activates latent HIV-1 by increasing NF-κB activity without affecting DNA modification. Combining PKC412 with the HDAC inhibitor vorinostat has a synergistic effect on HIV-1 reactivation in both ACH2 cells and latent infected PBMCs.

Conclusions: we have identified PKC412 as a novel compound that has the potential for optimization and development as a latency-reactivator for eradicate HIV-1 infection.

BSP5.04

Longitudinal Quantitative Proteomics Study of Gut Dysfunction during Acute SIV Infection in Rhesus Macaques

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HIV infection damages tight epithelial barriers of the gut mucosa leading to increased morbidity. Current HIV therapies do not restore mucosal health as the mechanism of gut dysfunction is unknown. We hypothesize that tight junction stabilization proteins are altered early on in infection and contribute to dysfunction, however early kinetics of these alterations have not been studied. Here we utilized a proteomics approach to characterize early molecular changes during acute SIV infection in a rhesus macaque model.

Methods: Gut (colon) tissue biopsy samples from 6 SIV infected macaques were analyzed by label-free mass spectrometry to evaluate longitudinal host protein changes after infection. Tissues were extracted at days -56, -21, 3, 14, 28, 63 from challenge, and day of necropsy. 921 proteins were identified at 25% covariance (CV) between technical replicates. Differential protein expression post-SIV challenge were analyzed using paired t tests ($p<0.05$ w/ 5% FDR cutoff) relative to baseline (-56, -21). Data was analyzed using IPA pathway software.

Results: Protein expression significantly changed over time including 1 protein at Day 3, 16 proteins at day 14, 9 proteins at day 28, and 9 proteins at day 63. The top biological functions affected during early infection, identifying novel transcription factors, were cell development ($p<0.001$), and infectious diseases/antiviral responses ($p<0.0001$) which indicates host reaction to infection. At later time points, functions in integrity of adherens junctions ($p<0.01$), wound signaling proteins, and tight junction proteins were differentially expressed indicating gut dysfunction. Cell death pathways ($p<0.00001$) were highly activated at late time points, a known driving force of early infection pathology. The tight junction alterations and novel transcription factors affected prior to epithelial dysfunction may be early signals or drivers of inflammation important for barrier disruption and represent new targets for mechanistic studies.

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BSP5.05

Optimisation of the TILDA assay for the quantification of HIV reservoirs

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The major obstacle in the eradication of the HIV virus is the quantification of the latent HIV reservoirs. There are many PCR-based HIV viral load quantification methods and the gold standard technique is the quantitative Viral Outgrowth Assay. Recently, we have described a new PCR-based assay, named the Tat/Rev Induced Limiting Dilution Assay (TILDA). TILDA measures the frequency of latently HIV-infected $CD4^+$ T cells actively producing multiply spliced RNA coding for the Tat/Rev genes.

Here in this study we wanted to further optimize the assay by investigating the impact of different factors such as: the volume transferred from the first PCR plate to the second, storage of PCR plates in -20˚C between the PCR runs and the amount of cells in the PCR wells. We used RNA extracted from the reference latently HIV-infected ACH2 T cell line which contains one proviral HIV DNA per cell, to spike CD4+ T cells and monocyte-derived macrophages (MDM) isolated from PBMCs from healthy donors with known quantity of RNA extracted from ACH2 cells.

Based on our findings we recommend the following modifications to the current TILDA protocol: 1) transferring 2µl from the first PCR plate to the second instead of 1µl and 2) no delay between the first and second PCR run (plates should not be frozen). Also we found that the assay was not accurate when 18,000 MDMs or more were added to each wells. Therefore, the TILDA assay would not be the best method to quantify latent viruses in the macrophage reservoir since it has been reported that the IUPM in macrophages is much lower than in $CD4^+$ T cells which would require adding more macrophages per well.

BSP5.07

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

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A major barrier to the eradication of HIV-1 infection was found with the discovery of latent HIV-1 proviral reservoirs. This reservoir is resistant to the effects of anti-retroviral drugs (ART) and primarily resides in resting CD4+ T cells to which ceasing ART therapy would cause an eventual viremic relapse. Eradication methods are currently studied, but issues arise with measuring the latent HIV-1 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 Viral Outgrowth Assay (VOA) 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 VOA.

The goal of this project was to further validate the MOLT-4 VOA. Using the latently HIV-infected CD4+ T cell ACH2 cell line as a reference material, we compared the results from the MOLT-4 VOA to the Standard VOA for their sensitivity in detecting 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 was 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 the standard VOA delivered the expected IUPM while the MOLT-4 assay was not as sensitive, giving a much lower IUPM.

In close, we recommend further validation of the MOLT-4 VOA assay before its use. As of now, the standard VOA remains the current culture-based assay to measure latent replication competent viruses.

BSP5.08

Variable Nef expression results in differences in Nef-mediated downregulation of MHC I and CD4 between HIV-1 subtypes

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Since its emergence, HIV-1 has undergone continuous selective pressure leading to a staggering degree of genetic diversity. However, HIV-1 research has largely been limited to only a few subtypes, failing to provide a complete understanding of the epidemic. We aimed to study the consequences of HIV-1 genetic variability on the viral accessory protein Nef. Nef is essential to HIV-1 pathogenesis in part due to its ability to mediate HIV-1 immune evasion and increase viral replication by downregulating cell surface receptors MHC I, and CD4, respectively.

In order to investigate Nef function across a diverse range of HIV-1 subtypes we measured cell surface MHC I levels in a human T cell line pseudoinfected with modified HIV-1 viruses expressing Nef proteins from 11 HIV-1 subtypes. CD4 cell surface levels were measured by transfecting $CD4^+$ HeLa cells with expression plasmids encoding Nef-eGFP fusion proteins. MHC I and CD4 downregulation efficiency was measured by flow cytometry and results demonstrate these receptors are differentially downregulated between subtypes. We have identified a subset of low functioning Nef proteins from subtypes C, G and H that are poorly expressed, suggesting a mechanism for decreased receptor downregulation. Decreased Nef expression from these subtypes was consistent between independent expression systems and was not due to differences in transcription, as these subtypes had equivalent mRNA levels to high expressing subtypes. In addition, we identified the potential genetic determinants of decreased Nef expression in HIV-1 subtype C, the most prevalent subtype in the HIV/AIDS epidemic.

Our study represents a comprehensive analysis of Nef function among HIV-1 subtypes and suggests differences in expression of the viral accessory protein Nef across HIV-1 subtypes, which may play a role in intersubtype differences in disease progression.

BSP5.09

Lentiviral Counteraction of Oncogenic APOBEC3 Proteins

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Mutations can be harmful, or helpful. The APOBEC3 family of proteins are DNA cytosine deaminases that can instigate mutations in DNA. When the source of this DNA is our own human cells, mutation can lead to cancer. When this DNA

is found in pathogenic viruses, mutation can halt viral replication. For example, APOBEC3D, APOBEC3F, APOBEC3G, and APOBEC3H combine to restrict HIV-1 in human lymphocytes. HIV-1 counteracts these APOBEC3s with the viral protein Vif, targeting them for proteasomal degradation. However, the oncogenic APOBEC3 proteins (APOBEC3A and APOBEC3B) do not restrict HIV-1 and are not targeted by HIV-1 Vif in CD4-positive T cells. Here, we investigate the possibility that other lentiviruses are targeted by the analogous APOBEC3 proteins of their host species, and have evolved a conserved counteraction mechanism. These findings will enable us to take advantage of virally-evolved defenses in order to counteract human cancers.

BSP5.10

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

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Background: The ability of HIV to establish and persist within cellular reservoirs as a transcriptionally silent provirus represents substantial roadblocks to cure research. Therapeutic interventions designed to eliminate this hidden reservoir have thus far failed, and may require bold and innovative strategies. Our activator vaccine (ACT-VEC), based on autologous derived VLPs, targets the resting CD4 T cell reservoir, and induces latency reversal.

Methods: Macaques were divided into 4 groups (n=2), groups 1 and 2 previously received a proprietary CTL vaccine, groups 3 and 4 acting as non-CTL vaccinated controls. Macaques were administered daily cART (FTC+PMPA+Raltegravir) for 1 year to suppress viral replication. ACT-VEC vaccinated macaques received four, monthly, 90ug and 10ug concurrent intramuscular and intra-lymph node vaccinations. Antiretroviral therapy was continued for one month post the final ACT-VEC vaccination then treatment was withdrawn, and viral rebound assessed by PCR. Blood draws were taken throughout the study for assessment of anti-HIV antibody responses as well as T cell immune responses.

Results: Two macaques (one placebo, one ACT-VEC treated), were euthanized due to weight loss associated with acute renal toxicity through the cART regimen. Another macaque was removed from the placebo group upon cART cessation due to "Elite" control of viremia. In total 3 ACT-VEC vaccinated and two placebo control macaques were assessed in this study. While all macaques experienced viral rebound, a 10-20 fold reduction in viral rebound in ACT-VEC treated groups compared to only 3-8 fold reduction in the placebo arm.

Conclusion: The results presented reveals that ACT-VEC might impact the magnitude of viral rebound upon cART cessation. Further work is needed to affirm this the results of this proof of concept study. Additional planned analysis of immunological parameters will greatly improve our understanding of the vaccine and help verify whether any protective effect was realized.

BSP5.11

Dynamics of DC:T cell interactions and their implications on HIV-1 dissemination

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The development of antiretroviral therapy (ART) is a great achievement in modern medicine, significantly prolonging the life span of infected individuals and reducing AIDS-related mortality. However, ART is not curative, as evidenced by the rapid rebound in viremia seen in patients after therapy interruption, despite months of undetectable viremia. One possible explanation is the presence of viral reservoirs in various tissue compartments, serving as depots for latently infected cells that can spontaneously reinitiate virus production. Alternatively, viral replication may persist at low levels in tissues where drug bioavailability is suboptimal. Recent findings show that ARTs are less effective at suppressing HIV infection when the virus is transmitted through direct cell-to-cell contact between infected and uninfected cells. Given the densely packed nature of lymphoid tissues, where explosive viral replication occurs, it is conceivable that cell-to-cell HIV-1 transmission plays an important role in viral dissemination *in vivo*. Here, we provide new insights into the cellular dynamics and molecular mechanisms of HIV-1 spread through DC:T cell interactions within physiologically relevant, 3D environments. Using live-cell imaging approaches and a panel of fluorescent-reporter HIV-1 strains, we demonstrate that HIV-infected DCs frequently contact susceptible T cells in an Env-dependent manner. Data on the frequency and kinetics of viral transfer will be presented.

BSP5.12

Insulin suppresses virus replication and neuroinflammation with improved neurological outcomes in models of HIV/AIDS

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Background: HIV-1 infection of the brain causes neuroinflammation and contributes to the development of the neurodegenerative syndrome, HIV-associated neurocognitive disorder (HAND), which affects 25% of HIV/AIDS patients receiving combination antiretroviral therapy. Insulin resistance is associated with chronic inflammation and has become a major complication of contemporary HIV/AIDS care. Earlier studies report that insulin treatment suppress-

es HIV-1 replication in cultured leukocytes. We investigated insulin receptor expression and the neuroprotective effects of insulin in *in vitro* and *in vivo* models of HAND.

Methods: Host and viral gene expression was analyzed in cultured human microglia following HIV-1 infection, in autopsied human and feline brain specimens by RT-PCR, ELISA, and immunohistochemistry. Cats infected with a neurovirulent feline immunodeficiency virus (FIV) were examined using neurobehavioral, immunological and molecular tools.

Results: Despite increased neuroinflammatory gene expression in brains from patients with HIV/AIDS, both insulin and IGF-1 receptor expression was unaffected but PPAR-γ expression was reduced by HIV-1 infection. HIV-infected primary human microglia (HFM) showed reduced HIV-1 p24 levels in supernatants following insulin treatment in a concentration-dependent manner. Insulin treatment of HIV-infected HFM suppressed CXCL10 and IL-6 transcript levels while PPAR-γ expression was induced. Insulin treatment of human neurons reduced HIV-1 Vpr–mediated neurotoxicity. FIV-infected (FIV[+]) cats were treated (6 weeks) with intranasal insulin (20.0 IU/200 mcl) or vehicle (PBS, 200 mcl). Insulin treatment suppressed cortical CXCL10 and IL-6 expression in FIV[+] animals together with reduced FIV transcript and protein levels although PPAR-γ levels in glia were increased by insulin treatment, compared to vehicle-treated FIV[+] animals. These molecular changes were accompanied by reduced gliosis and improved neurological status including both memory and motor functions in the insulin-treated FIV[+] group.

Conclusion: Insulin exerted *in vitro* and *in vivo* antiviral and anti-inflammatory effects in models of HAND, representing a new therapeutic option for patients with HAND.

BSP5.13

In vitro assessment of the function of naturally occurring Vpu sequences without codon optimization or rev-dependent expression

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Background: The HIV-1 accessory protein Vpu exhibits high inter- and intra- subtype genetic diversity, but methods to evaluate genotype/phenotype correlations of natural Vpu sequences are limited. Historically, *in vitro* Vpu expression requires codon-optimization (which precludes assessment of natural sequences) or cloning of substantial upstream information into plasmids that incorporate cis-acting elements and co-express Rev (which could introduce genetic incompatibilities between the Vpu insert and plasmid backbone). We describe an assay to measure two well-characterized Vpu functions, Tetherin and CD4 downregulation, in immortalized T-cells, via direct cloning of the Vpu coding region to circumvent these limitations.

Methods: HIV-1 NL4.3 (subtype B), MJ4 (subtype C) and codon-optimized (CO) Vpu were cloned into an expression plasmid co-expressing GFP (pSELECT) with and without a 3' FLAG tag. These alleles were also engineered as GFP fusions. NL4.3 and MJ4 Vpu were also cloned into pSELECT with ~50 and ~100bp of upstream noncoding sequence. NL4.3 Vpu (along with the required ~100bp of upstream sequence) was also cloned into a Rev-expressing plasmid for comparison. Vpu clones were transfected into an immortalized CD4+ T- cell line, and Tetherin and CD4 downregulation were assessed by flow cytometry. Vpu expression was assessed by western blot and confocal microscopy.

Results: When Vpu was cloned directly at the start site, NL4.3 and MJ4 displayed lower yet consistently measurable downregulation function compared to the CO allele. This NL4.3 Vpu clone functioned similarly when the allele was cloned into a Rev-dependent system. NL4.3 Vpu function was maintained with a 3' FLAG tag. However, inclusion of upstream noncoding sequence or a C-terminal GFP fusion abrogated NL4.3 and MJ4 Vpu expression in pSELECT.

Conclusion: The function of natural Vpu sequences can be assessed *in vitro* without codon optimization or Rev co-expression if Vpu coding regions are expressed without upstream viral sequences or as large fusion products.

BSP5.14

Stimulation of HIV transcription by virion-associated envelope glycoprotein (gp120) through manipulating different cellular machineries

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Introduction: HIV-1 infection *in vivo* is characterized by persistent high-level viral replication associated with rapid turnover of CD4+ T cells. Meanwhile, the virus infected resting CD4 T cells also constitute a major long-lived viral reservoir, especially under antiretroviral therapy. However, the mechanisms of why HIV can replicate aggressively *in vivo* and also, when ART was interrupted, the viral replication rapidly rebounds are still not fully understood. Previous studies suggested that HIV envelope is able to mediate a cascade of cell signals and facilitate the virus replication in non-proliferating target cells. The present study investigated the effects of HIV envelope glycoprotein (gp120) present on defective particles on HIV transcription and expression, especially in resting CD4+ T cells and elucidated the underlying mechanism.

Results and Conclusions: We first demonstrate that HIV gp120 presented on the "defective particles" (Env-VLP) significantly activates HIV transcription in 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 gp120 and CD4 and coreceptors (CCR5 or CXCR4) and is Tat independent. Through the use of RNA transcriptome sequencing, we identified more than 100 genes that were significantly modulated in response to Env-VLP treatment. Among these genes, one was microRNA181A2. Env-VLP treatment lead to a downregulated of microRNA181A2 and consequently the upregulation of P300/CBP-associated factor (PCAF), that results in an enhanced LTR histone H3 acetylation and HIV transcription. Overall, these observations provide evidences to support that virion-associated gp120 can activate viral transcription by manipulating cellular pathways and contribute to the maintenance of HIV production in and from viral reservoir.

BSP5.15

Single-Particle Characterization of MLV and HIV by Flow Virometry

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Improvements in flow cytometer optics and instrumentation now allow for the detection of particles down into the 80-100nm size range. These advances have made it possible to analyze viruses at the single particle level in a high-throughput fashion, a process previously only applied to much larger particles, such as eukaryotic cells and bacteria. These new advancements thus allow for the characterization of antigen expression levels on intact virus particles, termed flow virometry. For the first time, we have analyzed Murine Leukemia Virus (MLV) and Human Immunodeficiency Virus type I (HIV-1) virions by flow virometry. This method was applied to illustrate differential surface density of an eGFP-envelope glycoprotein fusion (Env-eGFP) on individual viral particles of two variant strains of MLV. Interestingly, we also characterized HIV-1 particles by analyzing gp120 density on individual virions using fluorescently labeled soluble CD4. In addition, we have evaluated the sensitivity of these techniques to visualize intravirion material, including packaged host proteins. Finally, our methods are also uniquely capable of distinguishing the parent cells of progeny virus using distinct membrane labels. The development of these protocols constitute a significant advancement in the field of virology which enable researchers to distinguish viral species and sub-populations, cellular origins of infection, tropism and protein content from a variety of sample sources, including blood from infected individuals.

BSP5.16

Characterizing the impaired type I interferon response in HIV-infected myeloid cells

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Introduction: A number of immune evasive strategies, including impairment of the antiviral type 1 interferon (IFN1) response, are believed to facilitate HIV replication and viral spread. As defects in the IFN1 response have been exploited in the development of novel cancer therapies, the same may hold true for HIV/AIDS. However, IFN1 signalling in the context of persistent infection, such as that seen in HIV-infected macrophages, remains poorly understood.

Hypothesis: IFN1 responses are impaired during persistent HIV infection of myeloid cells.

Methods: The latently HIV-infected cell line, U1 and its uninfected parental cell line, U937, as well as *in vitro* HIV-infected, monocyte-derived macrophages (MDMs) were studied. Surface expression of the IFNα receptor (IFNAR) was first measured. Then, following 24 hours of stimulation with either IFNα, or the synthetic RNA, poly(I:C), the expression of various IFN stimulated genes (ISGs), including PKR, ISG15, and MHCI, was measured by flow cytometry.

Results: IFNAR expression at basal levels, and in response to IFNα, was lower on latently HIV-infected U1 cells in comparison to uninfected U937 cells. Furthermore, following IFNα or poly(I:C) stimulation, the induction of PKR and ISG15 expression was greater in U937 cells than in the latently infected U1 cells. In uninfected MDMs, treatment with IFNα or poly(I:C) induced ISG15 expression in a dose-dependent manner. The study of potential IFN1 signalling defects in HIV-infected MDMs, treated with either IFNα or poly(I:C), is ongoing.

Conclusions: In comparison to uninfected U937 cells and MDMs, IFNAR expression and ISG induction was impaired in the latently HIV-infected, pro-monocytic U1 cells. These findings suggest that, similar to productive HIV infection, latent infection may be associated with defects in the IFN1 response. Additional studies will serve to characterize IFN1 responses within HIV-infected MDMs, and determine how potential defects may be exploited for the development of novel therapies.

BSP5.17

Slow disease progression of women infected with HIV-1 subtype C versus subtype A and D: Implications for the epidemic

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Background: The progressive loss of $CD4^+$ T Cells during HIV-1 infections are powerful predictors of disease progression and time to the onset of AIDS. However, infections

by distinct subtypes of HIV-1 Group M display differing degrees of pathogenicity. The predominant viral subtypes of the epidemic in Sub-Saharan Africa are A, D and C, with subtype C making up more than 50% of global infections alone. Unfortunately, despite their importance in global health, these subtypes understudied relative to subtype B. This study sought to compare rates of pathogenesis and rates of entry between these understudied viral subtypes using clinical data and primary isolates from a natural history cohort.

Results: These data showed distinct patterns of T cell decline between HIV subtypes. Infection with a subtype C virus shows a significantly slower rate of cell decline in both total $CD4^+$ cells as well as in $CD4^+$ memory subsets compared to subtypes A and D ($p<0.01$ and $p<0.003$ respectively). Additionally, subtype C infections demonstrate a significantly longer time to viral load set point with no difference in total viral load at set point relative to subtypes A and D ($p=0.009$ and $p<0.001$ respectively). Finally, two models of Env mediated cellular entry demonstrate subtype C Envs bind and fuse at a slower rate than compared to subtypes A and D ($p<0.0476$ and $p<0.0002$ respectively).

Conclusions: Disease stemming from infection by an HIV subtype C virus progresses at a diminished rate compared to subtypes A and D. Our data also suggest that similar patterns are also true for viral entry and syncytia formation; subtype C viruses bind and enter cells at a diminished rate relative to subtypes A and D. Future work will investigate the induction of CD4+ cell death caused by viral envelopes between differing HIV-1 subtypes across memory CD4+ T cell subsets.

BSP5.18

The V3 Loop of HIV-1 Env Regulates Virus Susceptibility to IFITM Inhibition

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Interferon Inducible Transmembrane Proteins (IFITMs) inhibit a broad spectrum of viruses including HIV-1. In addition to impairing HIV-1 entry when being expressed at the surface of virus target cells, IFITM3 is incorporated into HIV-1 particles and diminishes viral infectivity by abrogating the processing of viral Env protein. In this study, we have tested several HIV-1 primary isolates for their susceptibility to the IFITM3 inhibition of viral infectivity, these include 89.6, Yu-2 and AD8.1 in addition to the lab adapted strain NL4-3. The IFITM3 plasmid DNA was co-transfected into HEK293T cell together with each of these viral DNA clones. Examining the virus particles revealed that the IFITM3 protein was incorporated into all of these four viruses, yet the infectivity of AD8.1 and YU-2 was not affected by IFITM3 as opposed to a severe decrease in the infectivity of NL4-3 and 89.6. By studying a chimeric virus that had the Env sequence of AD8.1 inserted into the NL4-3 DNA, we observed that this chimeric virus called NL(AD8Env) became refractory to IFITM3 inhibition. Results of further mutagenesis showed that inserting the V3 loop sequence of AD8.1 Env into NL4-3 Env was sufficient to confer resistance to the inhibition by IFITM3. We also replaced the V3 loop sequence of NL4-3 Env with those of other HIV-1 strains and observed different degrees of inhibition of these viruses by IFITM3. Together, these observations suggest that the V3 loop of Env provides a mechanism allowing HIV-1 to overcome the IFITM3 restriction.

BSP5.19

Investigation of the effect of IL-34 on HIV-1 infection in CD4+ T lymphocytes, matured macrophages and underlying mechanisms

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Background: Interleukin-34 (IL-34) is one of the two identified ligands of CSF-1R, which mainly produced by T-cells, monocytes, macrophages and endothelial cells. Recent studies showed that IL-34, produced by mouse follicular DCs in germinal centers, is able to promote the differentiation of Lin-, c-kit+ spleen cells into monocytic cells, which in turn, stimulate activated B cell proliferation. Interestingly, recent studies also revealed that the presence of IL-34 induce the maturation of macrophages and increase HIV replication level in these cells. However, whether the IL-34 plays any role during HIV infection in CD4+ T lymphocytes is still elusive.

Results and Conclusions: In this study, we have investigated the effect of IL-34 on HIV replication in human PBMCs, purified CD4+ lymphocytes and macrophages. The results showed that, in addition to promote the differentiation of macrophages, IL-34 also stimulated HIV infection and production in the matured macrophages. More interestingly, our data revealed that in the presence of IL-34, the replication levels of T-tropic HIV in non-stimulated PBMC and purified CD4+ cells were significantly higher. These results suggest that that IL-34 may activate CD4+ lymphocytes to increase their susceptibility to HIV infection or act directly on HIV replication in CD4+ lymphocytes. More detailed studies are underway for better understand the roles of IL-34 in HIV replication and its pathogenesis.

Lab Testing and Monitoring
Épreuves de laboratoire et surveillance

BSP6.01

HIV Drug Resistance Mutation Genotyping from Low Viral Load Specimens Stored as Dried Blood Spots

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Background: Plasma is the most desirable specimen type for HIV drug resistance genotyping. However, it may not always be possible to collect plasma in resource limited settings. Dried blood spots (DBS) are a suitable alternative because (1) collection requires minimal equipment, (2) storage and transportation does not require refrigeration and (3) genotyping results are comparable to those observed with plasma. The World Health Organization defines a viral load of over 1,000 copies/mL in plasma at 12 months post commencement of antiretroviral therapy, as an indicator for drug resistance genotyping. As a result, robust methodology is critical for successful HIV drug resistance mutation genotyping from DBS due to the low volume of blood collected.

Methods: Whole blood was spiked with cultured HIV from the External Quality Assurance Program Oversight Laboratory. Spiked whole blood was prepared at a viral load of 10,000 to 500 copies/mL and spotted onto Whatman 903 cards. Nucleic acids were extracted using an easyMAG instrument. *Protease* and part of the *reverse transcriptase* genes were amplified using an in-house HIV genotyping assay.

Results: See table 1

Conclusions: Nucleic acids can be reliably amplified from HIV specimens stored as DBS for the purpose of drug resistance mutation genotyping at a viral load of 1,000 copies/mL or higher. PCR amplification was much less reliable and success rates dropped considerably below 1,000 copies/mL. The performance of our in-house HIV genotyping assay is comparable to other laboratories within the WHO Global HIV drug resistance network.

Table 1 – PCR Amplification Success Rates

	HIV subtype				
	B (n=14)	C (n=9)	A1 (n=14)	CRF01_AE (n=4)	CRF02_AG (n=3)
Protease					
10,000 copies/mL	95.2%	100.0%	86.7%	100.0%	66.7%
5,000 copies/mL	92.9%	88.9%	100.0%	91.7%	66.7%
1,000 copies/mL	71.4%	59.3%	60.0%	100.0%	88.9%
500 copies/mL	40.5%	48.1%	40.0%	75.0%	0%
Reverse Transcriptase					
10,000 copies/mL	92.9%	92.6%	100.0%	100.0%	66.7%
5,000 copies/mL	92.9%	85.2%	100.0%	100.0%	88.9%
1,000 copies/mL	71.4%	70.4%	66.7%	100.0%	100%
500 copies/mL	50.0%	51.9%	80.0%	91.7%	33.3%

BSP6.02

Evaluation of the Pima Analyser for CD4 enumeration in HIV patients

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Background: The Pima Analyser is one of the Point Of Care (POC) technologies currently available to enumerate the absolute number of T-helper cells (CD4+) in the field of HIV/AIDS. For many resource-limited countries, CD4 immunophenotyping remains the way to assess HIV disease state and to determine eligibility for antiretroviral treatment. In an attempt to address this issue, we conducted a study to validate the performance of the Alere PIMA POC CD4 analyzer.

Method: We collected 100 adult HIV+ fresh whole blood samples from patient populations attending Ottawa and Winnipeg hospitals (Canada). These samples were collected with K3 EDTA-containing tubes and tested after 24h with 3 instruments:2 Alere PIMA analyzers and the Becton Dickinson FACSCalibur as a reference instrument.

Results: CD4 counts by Pima correlated well with those from FACSCalibur with an R^2 of 0.96 for Pima 1 and 0.97 for Pima 2. Both Pima instruments underestimated CD4 absolute count measurements compared to the FacsCalibur with a bias of -17 cells/ml for Pima 1 and -26 cells/ml for Pima 2. The bias was seen in samples with CD4 counts below ≤350 cells/µl (Pima1 = -2 cells/ml, Pima 2= -11 cells/ml) and in the CD4 >350 cells/µl stratum (Pima1 = -32 cells/ml, Pima 2=-41 cells/ml). The variation around the bias (SD and limits of agreement) was similar for both Pima units according to the CD4 stratum. In terms of repeatability,

both Pima units had an acceptable coefficient of variation (CV) compared to the values of the company.

Conclusion: As previously demonstrated, this study demonstrates that the Pima analyzer is adequate for HIV clinical management. This POC will be a feasible alternative to a large flow cytometer for CD4 enumeration, particularly in clinical laboratories from limited-resources settings.

BSP6.03

Comparison of two HTLV confirmatory assays : INNO-LIA™ HTLV I/II Score and in-house HTLV-I RIPA

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Objective: Compared to HTLV-I which is associated with T-cell leukaemia and HAM/TSP, HTLV-II is an infectious agent looking for a disease. Although little is known, the virus may be especially prevalent in high-risk groups such as intravenous drug users. The NLHRS evaluated its current HTLV-I/II algorithm for samples received for confirmatory testing from Canadian laboratories.

Methods: The NLHRS uses two confirmatory assay for HTLV-I/II diagnostics; Fujirebio® INNO-LIA™ HTLV I/II Score assay and in-house HTLV-I radiommunoprecipitation (RIPA). If the test results are discordant, the sample is reported as indeterminate and requires PCR testing. Results from clinical samples submitted to the NLHRS from 2013-2015 were examined retrospectively for discrepancy between the assays.

Results: Of the 36 HTLV-II antibody positive samples by INNO-LIA™, 13 (36.1%) were negative and only 2 (5.6%) were positive on HTLV-I RIPA. The remaining 21 (58.3%) were indeterminate. In the case of HTLV-I antibody positive samples by INNO-LIA™, 105 (74.5%) were positive and 3 (2.1%) were negative on HTLV-I RIPA. The remaining 33 (23.4%) were indeterminate. Out of the 232 that tested negative by INNO-LIA™, 226 (97.4%) were tested negative, 6 (2.6%) were indeterminate and none tested positive by HTLV-I RIPA. Of the 16 untypeable samples by INNO-LIA™, 12 (75%) were negative and 4 (25%) were indeterminate on HTLV-I RIPA. Of the 39 indeterminate samples by INNO-LIA™, all were negative on HTLV-I RIPA.

Conclusion: The results illustrate that the HTLV-I RIPA was not efficient in resolving HTLV-II antibody status compared to INNO-LIA™. This resulted in increased turn-around time since additional testing was required. In addition, there may be a sensitivity issue with HTLV-I RIPA because only 75% of the INNO-LIA™ HTLV-I positives were positive by RIPA. Re-evaluation of the NLHRS HTLV serology algorithm may be needed.

BSP6.04

Modernizing the data reviewing strategies for enhanced HIV virology quality assurance in next generation sequencing era

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Background: HIV virology quality assurance(VQA) programs administered by WHO or NIH are commonly applied for validation of Sanger sequencing(SS)-based HIV drug resistance(DR) assays or performance assessment of HIV DR laboratories. VQA proficiency panel samples are tested in participating labs and the derived sequences are then submitted and assessed against the "consensus" generated by using an 80% threshold from the alignment of all submitted sequences. Although widely applied, issues remain regarding the appropriateness of such data assessment strategies and many sites with "ambiguous" bases have to be excluded from analysis. In the era of next generation sequencing (NGS), it becomes feasible to quantitatively pre-determine the genotype/phenotype(GT/PT) at all loci in VQA samples and use such data for VQA data assessment while taking the intrinsic limitation of SS into consideration.

Methods And Results: Four samples from the VQA panel GEN028DR were re-sequenced using Illumina MiSeq, an exemplar NGS technology, and the frequencies of all GT/PT variations across the examined genes were recorded. All 49 VQA submissions on these samples were then re-examined for the reported GT/PT discrepancies among the submission. Not surprisingly, 90.1% and 89.9% of the GT and PT discrepancies were observed within the frequency ranges of 12% and above respectively, which reflects the intrinsic limit of any SS methods. By using the GT/PT frequency data from NGS as standard, a refined VQA data reviewing strategy is proposed to more objectively and quantitatively assess the ability of a protocol/laboratory to detect GT/PTs at varied levels.

Conclusions: NGS characterization of VQA proficiency samples and using such data for final VQA scoring helps to assess the submissions more precisely and objectively as compared to the conventional Sanger-consensus approach. It is suggested that such a strategy should be implemented in routine VQA programs.

BSP6.05

What impact does plasma storage temperature have on HIV-1 viral load quantification?

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Background: In HIV-1 viral load testing, the standard protocol is to use plasma/sera stored at ultralow temperatures (-80˚C). There is little information on the impact of alternative storage temperatures on quantification. The NLHRS used data from its proficiency testing program to examine the effect of storage temperature compared to the standard -80˚C (-20˚C for 13 months, 8 months, 35 days and 5 freeze/thaws).

Methods: One HIV-1 RNA subtype B sample (~1000copies/mL) was aliquoted and stored in duplicate under the various storage temperatures. Canadian and international labs tested the samples on the Roche CAP/CTM HIV-1 Test v2.0 or Abbott RealTime HIV-1 assay during 3 proficiency test events.

Results: On the Roche assay, samples at all storage temperatures including -80˚C, generated a viral load range >0.5 log. Conversely, only samples stored at -20˚C for 13 months had a range >0.5 log on the Abbott assay. The Roche assay did not show a significant difference for any of the storage temperatures compared to -80˚C ($p>0.11$) but the intra-sample variation was high. While the Abbott assay showed a significant difference for storage at -20˚C for 8 months and 5 freeze/thaws compared to -80˚C ($p<0.02$), the intra-sample variation was still within 0.5 log. Overall, the viral loads on the Abbott assay were lower than the Roche assay and had a tighter range.

Conclusions: Our data suggests samples stored at -20˚C for up to 8 months, compared to -80˚C, will still yield results within 0.5 log on the Abbott assay. This may be beneficial if laboratories do not have access to ultra-low freezers and/or inadvertently stored samples above -80˚C. The wide range between samples (>0.5 log) on the Roche assay at all storage conditions is troublesome as acceptable variation is generally ≤0.5 log. Further investigation in storage methods is warranted based on these findings.

BSP6.06

Specimens from Pregnant Women yielding False-Reactive Results on the Abbott Architect HIV Ag/Ab Combo Assay Leading to mis-Diagnosis and Negative Patient Impact

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Background: Serological testing for HIV remains an effective and cost-effective screening method to reduce the number of specimens requiring confirmatory testing. Fourth (4th) generation immunoassays, which now include the ability to detect HIV-1 p24 antigen, have reduced the window period, bringing it closer to HIV-1 nucleic acid tests (NAT). Here we present results on reference specimens from pregnant women initially tested repeatedly-reactive on the Abbott Architect HIV Ag/Ab Combo assay which were ultimately confirmed as HIV-negative.

Methods: Sample criteria included: (a) specimens from provincial public health laboratories that were reactive on the Abbott ARCHITECT and (b) diagnosed HIV-negative by the NLHRS via its serology and/or PCR testing algorithm. These specimens were then tested on an alternative 4th generation Combo test (Siemens ADVIA Centaur HIV Ag/Ab Combo Assay).

Results: All specimens from pregnant women who initially tested repeatedly-reactive on the ARCHITECT, including several with S/Co values of 50-500, tested negative on the NLHRS serology and/or PCR algorithms. Serologic assays included alternative confirmatory assays (radioimmunprecipitation (RIPA), Fujirebio Inno-Lia HIV and Bio-Rad Geenius). PCR testing included the Roche CAP/CTM HIV-1 qualitative assay and 4-7 different in-house PCR tests for HIV-1/2. S/Co values on the Siemens assay were well below 1.0; consistent with values from HIV-negative specimens.

Conclusion: According to the new CLSI M-53 algorithm, a sample is first tested on a 4th generation HIV combo immunoassay. This test should have very high sensitivity *and* high specificity to ensure that truly positive specimens are not missed and truly negative specimens are not further tested. Here we demonstrate that specimens from pregnant women may generate false reactive values when tested on the ARCHITECT platform. The cause of this cross reactivity is under investigation. Finally, mis-diagnosis in these scenarios lead to overall frustration, increased turn-around-time for entry into care and treatment and increased testing costs.

BSP6.07

Development and Validation of a Whole-Genome Sequencing and Analysis Pipeline for the Clinical Testing of HTLV-I Positive Patients

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Introduction: The human T-cell lymphotropic virus type I (HTLV-I) is a human retrovirus and the causal agent of adult T-cell leukemia and HAM/TSP (HTLV-I-associated myelopathy/tropical spastic paraparesis). With an approximate 20 million people infected across the world, HTLV-I remains neglected in health care settings and under-characterized, as exemplified by the total number of available complete genomes on Genbank between HTLV-I (21) and HIV-1 (>4000). Whole-genome sequencing (WGS) is becoming

increasingly practical and accessible in diagnostic and reference laboratories due to decreasing costs. Here we present workflows that update existing HTLV-I subtyping methodologies and patient testing algorithms for HTLV-I positive patients, allowing for in-depth study of the molecular epidemiology of the virus.

Methods: Fifteen HTLV-I positive patient samples and the MT-2 cell line, used as a positive control, were extracted for high-molecular weight DNA and subjected to a single round of PCR. Two sets of primers were designed to specifically amplify two large amplicons (approx. 5500 bp and 4600 bp) that encompasses over 99% of the HTLV-I genome (9048 bp) with an overlap of 1 kb. Sequencing was performed on the MiSeq using the V3 (600-cycle) reagent kit. To estimate sequencing coverage, paired-end reads were initially pre-processed for read length and low quality trailing bases using Trimmomatic (version 0.35). The reads were mapped to a reference consensus sequence, generated from the 21 available HTLV-I whole genome sequences on GenBank, using Bowtie2 (version 2.2.6). Additional analyses performed *in silico* are forthcoming.

Results and Discussion: The Miseq generated an average of 770,997 reads per sample, with ~53.88% of reads mapping to the reference. Sequencing coverage for the sixteen samples commonly ranged from 3000-9000 across the reference genome. Forthcoming methods will compare mechanical (Covaris) and enzymatic (Nextera) shearing, and will fully utilize whole genome sequences for further characterization and study of HTLV-I molecular epidemiology.

BSP6.08

Comparison of Two Digital PCR Platforms and Development of an HIV-2 Quantitative Assay

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Background: Digital PCR (dPCR) is an interesting alternative to traditional quantitative real-time PCR because quantitation does not require standard curves. We present a comparison between the Bio-Rad QX200™ Droplet Digital™ PCR System and Life Technologies' QuantStudio™ 12K Flex Real-Time PCR System. Following the digital PCR evaluation, we developed an HIV-2 quantitative assay.

Methods: To compare digital PCR systems, an EQAPOL HIV-1 RNA and the WHO HIV-1 controls were extracted, amplified into cDNA, quantified and compared on the two different dPCR platforms. The HIV-2 quantitative assay used primers and probes targeting the gag region of HIV-2. A dilution series of 7 replicates using the WHO HIV-2 control was used to establish the lower limit of the assay.

Results: The quantification of the EQAPOL reagent was comparable to within 0.20 log of the previously calculated value for the control (68,700cp/ml [4.84]). Interestingly, when using a one-step RT-PCR system specific for each digital PCR platform a significantly lower quantitation was observed for the EQAPOL reagent on the QuantStudio™ 12K Flex Real-Time PCR System (24,193cp/ml [4.38]) and the QX200™ Droplet Digital™ PCR System (12,953cp/mL [4.11]).The WHO HIV-2 standard curve demonstrated that the assay was sensitive and reproducible. All 7 replicates at 125IU/mL were quantifiable. 6/7 at 62.5IU/mL and 4/7 at 31.25IU/mL were quantifiable therefore the lower limit of detection was then set at 100IU/mL.

Conclusion: All digital PCR systems evaluated gave comparable quantitation values for the HIV-1 controls. Finally, when quantifying RNA the choice of a 1-step or 2-step RT-PCR system may have significant impact on quantitation. Presently there is no quantitative HIV-2 assay commercially available. With the recent introduction of Bio-Rad's Automated Droplet Generator coupled with digital droplet PCR, we effectively identified HIV-2 in plasma as low as 100IU/mL. We have since been providing HIV-2 determinations to Canadian stakeholders.

BSP6.09

IL-33/sST2 axis in HIV Infection and its Correlation with Patient Outcomes and Markers of Gut damage

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Introduction: IL-33 is released as an 'alarmin' following cell necrosis to alert the immune system. Its receptor ST2 is implicated in microbial invasion, cytokine induction and promotion of cytotoxic CD8 T-cells. The soluble ST2 (sST2) form binds IL-33 as a decoy receptor to negate its inflammatory/healing effects. This study determined the relationship of the IL-33/ST2 axis with patient outcomes and gut mucosal markers.

Methods: We assessed 48 patients with early HIV infection (EHI), 61 with chronic HIV-infection (CHI), 21 elite controllers (ECs) and 20 controls. Prospectively, we assessed 17 EHI and 20 CHI patients initiating ART. IL-33 and sST2 plasma levels were compared with gut marker (I-FABP), microbial translocation (LPS, sCD14) and IDO immunosuppressive activity (Kynurenine/Tryptophan). CD4 and CD8 T-cell activation (HLADR/CD38) and exhaustion (PD-1) were assessed by FACS. IL-33 mRNA expression was assessed by qPCR.

Results: IL-33 plasma levels were close to the limit of detection in all groups as previously reported in auto immune disorders. We further report a similar mRNA expression in all groups. sST2 levels were elevated during EHI and CHI as compared to controls (18.6, 15.1 vs 11.7 ng/mL, $p<0.05$). sST2 levels during EHI positively correlated with plasma IDO activity ($r=0.324$, $p=0.026$) and CD8 count ($r=0.289$, $p=0.045$). However, no association of sST2 was observed with CD4 count and viral load. sST2 levels significantly correlated with CD4 & CD8 T-cell activation ($p<0.05$), I-FABP ($r=0.299$, $p=0.043$) and sCD14 ($r=0.369$, $p=0.012$). Prospective analysis following EHI showed that early ART had no impact on sST2 while it decreased in long-term treated chronic patients.

Conclusion: In contract to IL-33, sST2 was elevated in early HIV infection correlating with elevation of CD8 T-cell count and activation/exhaustion and with gut damage markers. By linking immune function and tissue damage, the IL-33/ST2 axis may induce gut injury and represents an important immunotherapeutic target.

BSP6.10

Bio-Rad Geenius™ HIV-1/2 versus Bio-Rad HIV-1/2 Multispot and Fujirebio INNO-LIA™ HIV I/II Score as a suitable confirmatory test for the CLSI-M53 HIV Guideline

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Background: The new CLSI-M53 HIV algorithm recommends an HIV-1 and HIV-2 discriminatory test to confirm samples initially reactive on an HIV 4th generation (Ab/Ag) EIA. This study compared the performance of the recently Canadian approved Bio-Rad Geenius™ HIV-1/2 confirmatory assay to the FDA-approved Bio-Rad HIV-1/2 Multispot rapid HIV test and the Fujirebio INNO-LIA™ HIV I/II Score.

Methods: Two-hundred and eighty-nine (289) well-characterized samples from Canadian stakeholder labs, commercial panels and negative samples obtained from a low-risk setting, were evaluated. All samples were assessed on the Bio-Rad Geenius™ HIV-1/2 and HIV-1/2 Multispot assays, which are rapid HIV tests that incorporate separate HIV-1 and HIV-2 antigens, either as distinct lines which are interpreted by an automated reader or as unique spots which are read visually. Problematic samples were further analyzed by the INNO-LIA™ HIV I/II Score assay.

Results: The overall performance of the Geenius™ and Multispot were very high; sensitivity (100%, 100%), specificity (96.3%, 99.1%), with positive (45.3, 181) and negative (0, 0) likelihood ratios, high kappa (0.96) and low bias index (0.0068). The ability to differentiate HIV-1 (99.2%, 100%) and HIV-2 (98.1%, 98.1%) antibodies was also significantly high. Where Geenius™ and Multispot revealed discrepant results, INNO-LIA™ HIV I/II Score was often able to correctly resolve the samples.

Conclusion: We have demonstrated that the recently approved Bio-Rad Geenius™ HIV-1/2 assay is a suitable assay to satisfy the CLSI-M53 HIV Guideline as an efficient new supplementary assay to discriminate between HIV-1 and HIV-2 antibodies. Furthermore, the test clearly exhibits operational advantages including the use of an automated reader and traceability features required of a quality management/assurance system. NLHRS has since incorporated this test into its reference testing algorithm, providing more rapid, accurate determinations to Canadian stakeholders.

BSP6.11

Point of Care Technology within the Quality Assessment and Standardization for Immunological measures relevant to HIV/AIDS (QASI) Program

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Background: QASI is an external quality assessment program for CD4 T-cell subset enumeration run by the Public Health Agency of Canada which aids with HIV disease-related immune status monitoring world-wide. Point-of-Care (POC) analyzers have been shown to significantly improve patient health through reduced test turnaround times and loss to follow-up by eliminating the need for significant infrastructure with stable electricity, highly trained personnel, regular instrument maintenance and cold-chain requirements. They are portable, low cost instruments.

Method: QASI participants are provided with an external quality assurance (EQA) panel comprised of 2 stabilized whole blood products with a high and low CD4 T-cell count 3 times per year for immunophenotyping and T cell enumeration.

Results: From 2010-2015 the number of participants using point-of-care analyzers to report absolute numbers of CD4+ T cells in the QASI program has risen from 4% to 59%. These participants reported comparable mean CD4+ results for the low and normal CD4+ count QC vs the QASI reference method (FACS Calibur) respectively. Robust group mean values were observed for both the low and normal CD4+ count QC samples across QASI sessions.

Conclusion: The performance of POC analyzers by QASI participants within our EQA program highlights its utility as an alternative rapid method for measurement of CD4+ T lymphocytes in HIV/AIDS patients in rural and remote locations.

Bacic Sciences Other
Sciences fondamentales, Autre

BSP7.01

A Social Networking Analysis of the Canadian HIV Vaccine Initiative Research and Development Alliance

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The renewed Canadian HIV Vaccine Initiative (CHVI) is a partnership between the Government of Canada and the Bill & Melinda Gates Foundation whose aim is to support and amplify national and international efforts to develop a safe and effective HIV vaccine. The cornerstone of the CHVI is the "Alliance network" which brings together leading researchers from the public and private sectors, as well as the national and international HIV community, to develop innovative solutions to the challenges facing HIV vaccine development. The core of the Alliance network is the CHVI R&D Alliance Coordinating Office (ACO) which provides a neutral platform through which the ambition of the Alliance can be translated into strategy, programs and performance. Recently Cathexis Consulting undertook a social networking analysis (SNA) of the Alliance membership to map out the connections of people and organizations within the network providing a mechanism through which the Alliance could be viewed and measured. The SNA examined several parameters including network density, distance, bridges and clustering. The SNA revealed that the Alliance network is moderately dense, its overall connectivity is very high however, there was significant clustering. Several of the large clusters identified are linked together primarily by a small group of high-status actors which include several ACO staff members. The SNA also showed that the Alliance network grew rapidly between 2012-2013 and 2014-2015 with increasing density and interconnectivity over time. The key findings indicate that the ACO has contributed to the considerable growth of the Alliance network by creating opportunities for linkages. Future growth of the Alliance may benefit from a conscious effort to increase network density while resisting the tendency for isolated clustering. These changes should result in an improvement in the sustainability of the Alliance particularly in the absence of key bridges and high status actors.

BSP7.02

Full-Length Ultra-Deep Sequencing Reveals Novel Alleles in SIVmac239 isolated from Non-Controller SIV-infected Cynomolgus Macaques

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Background: Next-generation sequencing (NGS) is a powerful tool used to produce extensive data and information on viral genomics such as low abundance viral variants and viral evolution. This study set out to comprehensively characterize the viral evolution of SIVmac239 isolated from non-controller SIV-infected cynomolgus macaques.

Methods: Cynomolgus macaques were previously utilized in an SIV vaccine study where half the animals were vaccinated with an SIV-VZV construct and the other half were controls. One year after vaccination, all animals were challenged intra-rectally with multi-low dose SIVmac239. Three phenotypes emerged; elite-controllers, controllers and non-controllers. In order to characterize SIV evolution within an infected host we isolated SIV from the infected plasma of the non-controller group at multiple time points over the course of a year and performed full-length SIVmac239 genome sequencing using the Illumina MiSeq platform.

Results: We analysed intra-host variability across the full genome and at specific CD8+ T-cell epitopes to identify polymorphisms at both the consensus and minor variant level. We observed several variants that occurred outside of known epitopes. These variants appear at different time points post-infection and approach fixation at different rates. One particular single nucleotide polymorphism (SNP) found at position 9263 in reference to GenBank: M33262.1 resulted a T→I change in rev, and a L→F change in env. This SNP was found in 100% of the non-controller group, and was absent in the elite and controller groups.

Conclusion: Preliminary analysis of intra-host evolution of SIVmac239 suggests that the formation of novel alleles is a unique process that occurs at varying kinetics and appears to be able to accommodate mutations that approach fixation in both structural and regulatory genes. Future studies will determine whether these mutations lie in novel epitopes and would implicate NGS as a valuable tool in aiding vaccine design.

BSP7.03

Connecting you to the Canadian HIV Vaccine Initiative Research and Development Alliance

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The renewed Canadian HIV Vaccine Initiative (CHVI) is a joint commitment between the Government of Canada and the Bill & Melinda Gates Foundation, aimed at supporting and amplifying national and international HIV vaccine research and development efforts. The cornerstone of the initiative is the CHVI Research and Development Alliance (Alliance), a partnership among Canadian funders, national and international researchers, community organizations as well as the vaccine industry. The core of the Alliance network is the CHVI R&D Alliance Coordinating Office (ACO) which provides a neutral platform through which the ambition of the Alliance can be translated into strategy, programs and performance. The ACO provides a variety of services to Alliance members including hosting webinars, workshops, consultations and virtual mini symposia as well as promoting, planning and facilitating HIV vaccine related events at national and international conferences. The ACO also provides networking opportunities, training, practicum placements and scholarships to new and early career investigators. The ACO has a variety of mechanisms through which it disseminates information including its website, e-bulletin, and social media networks. In addition, in order to build on existing collaborations and augment capacity building, the ACO has created the CHVI R&D Alliance Virtual Community (Alliance VC). The Alliance VC is a private internet-based community designed for groups and individuals working in the area of HIV vaccine research to collaborate, communicate, and share information. The Alliance VC provides a virtual meeting space for hosting "public" and "private" groups. It can also be used to facilitate online document creation and editing, organize teleconferences, and it houses a variety of resource materials including vaccine related reports, job postings, funding opportunities and a discussion forum. In summary, the ACO is committed to fostering innovative HIV vaccine research and development opportunities, supporting the coordination of funding and promoting international collaborations among Alliance members.

BSP7.04

The impact of the CIHR-funded International Infectious Diseases and Global Training Program on HIV research trainees from developing nations

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Introduction: To address the HIV pandemic, global and local approaches are needed to train new infectious disease scientists. One of the ways of meeting these goals is to have a critical mass of PhD trained researchers from developing countries where the impact of HIV is most dramatic, however, adequate training opportunities are often lacking. The Canadian Institutes of Health Research sponsored International Infectious Disease and Global Health Training Program (The Program) was designed to build research skills in Canadian as well as trainees in developing nations (Kenya, Colombia, India).

Approaches: Since 2009, The Program has not only recruited 21 trainees from Canada, but also 9 from Colombia, 12 from India and 11 from Kenya, most of whom were engaged in HIV research projects. Each trainee was matched with an internationally recognized mentor, trained on grant writing, participated in a monthly international scientific discussion forum and attended annual courses hosted in each country. Trainees were recruited from all 4 research pillars (basic, clinical, epidemiology, social) and all topics were approached from a multidisciplinary perspective.

Results: The Program currently has 14 international trainees from developing countries enrolled and has graduated 18. Success of trainees included securing highly competitive postdoctoral fellowships internationally, obtaining jobs in academia, and successfully obtaining local and international research grants. The 32 international trainees have produced 76 publications in peer review journals. In interviews with the trainees, they have indicated that The Program has contributed significantly to the skills needed for the next phase of their careers thereby providing them access to opportunities not previous possible.

Conclusion: In addition to training young Canadian researchers, the CIHR-International Infectious Disease and Global Health Training Program has contributed significantly to equipping international trainees with the high level knowledge and skills required to address the HIV epidemic challenges in their own countries.

Clinical Sciences

Sciences cliniques

Adherence
Respect du traitement

CSP1.01

Virtual nursing intervention (VIH-TAVIE) efficacy in empowering HIV patients to manage ART optimally: Quantitative and qualitative results

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Background: Exploiting the possibilities afforded by information and communication technologies, a virtual nursing intervention (VIH-TAVIE™) was developed to empower HIV patients to manage antiretroviral therapy (ART) optimally.

Objectives: A quasi-experimental quantitative study sought to compare the effectiveness of traditional and virtual (four VIH-TAVIE™ interactive computer sessions) follow-up in promoting ART adherence and a qualitative study aimed to understand how HIV patients experienced VIH-TAVIE™.

Methods: Participants were 179 HIV patients, of which 99 recruited at a site offering virtual follow-up and 80 at another offering only traditional follow-up. Primary outcome was medication adherence and secondary outcomes were self-efficacy, attitude toward medication intake, symptom-related discomfort, stress, and social support. These were evaluated by self-administered questionnaire at baseline and 3 and 6 months later. Semi-structured interviews were conducted with 26 participants who received all four VIH-TAVIE™ sessions.

Results: Participants had been with HIV for 14 years and on ART for 11. Baseline adherence was high, reaching 79.7% in the traditional follow-up group and 83.5% in the virtual follow-up group. A generalized estimating equations analysis was run. A time effect indicated both groups improved in terms of adherence over time but did not differ in this regard. Analysis of variance revealed no significant group-by-time interaction effect on any of the secondary outcomes. Content analysis yielded five themes regarding how HIV patients experienced VIH-TAVIE™: Exposure to VIH-TAVIE™; Virtual nurse humanizes the computer-delivered intervention; Learner's experience; Perceived benefits; Relevance of VIH-TAVIE™ in relation to the medication management trajectory.

Conclusions: Traditional and virtual follow-up have positive effects on adherence. Analyzing participants' experience of VIH-TAVIE™ revealed they found intervention content and format appropriate. To their eyes, the virtual nurse humanized the experience and helped them acquire new skills for achieving optimal ART adherence. VIH-TAVIE™ could constitute a complementary service in support of existing specialized services.

CSP1.03

Proving adherence to sexual abstinence after cervical biopsies performed in the context of basic science studies in female sex workers from Nairobi, Kenya

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Background: A better understanding of mucosal immunity must be achieved to develop an effective HIV vaccine. Cervical biopsies offer a unique opportunity for studying the local immune response, but caution must be taken to avoid HIV infection at the site of the wound. To investigate the cervical immune response of female sex workers (FSWs), we developed a biopsy sampling protocol. Here, we report on steps taken to minimize exposure to HIV during the sexual abstinence period following cervical biopsy sampling.

Method: Study participants were enrolled in two phases, 16 in Phase I, and 66 in Phase II. Two cervical biopsies were taken two weeks apart and women were asked to abstain from vaginal intercourse for 2 weeks after each biopsy to limit risk of HIV acquisition. In Phase I, women received counselling about HIV prevention and the importance of abstain from sexual intercourse during the healing period. As their primary income was from sex work, women were monetarily compensated for loss of income during that period. Despite the majority (82%) of participants' self-declaring full compliance to the abstinence period, we detected the presence of prostate-specific antigen (PSA) in 21% of the cervico-vaginal lavage collected. To improve compliance, we implemented additional preventive measures in the second phase. A comprehensive tool for informed consent, PSA rapid test performed on-site, and bi-weekly text message reminders were added to increase abstinence during the healing period. These activities significantly increased compliance to post-biopsy abstinence (91.1%) ($p=0.01$). There was no difference in the frequency of HIV target cells or expression of IL-8, MIG, MIP-1a and MIP-3a between the day of the first biopsy and one month later when the participants returned to sex work.

Conclusion: This study provides new tools for limiting HIV risk in studies requiring biopsy sampling among women at risk for acquiring HIV.

CSP1.04

Utility of a Brief Screening Intervention in Improving Depression and Antiretroviral Adherence in Patients with HIV

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Rationale: Given the efficacy of current antiretroviral (ARV) therapies, the strongest predictor of treatment success in patients with HIV is medication adherence. Studies suggest a negative association between depression and adherence, yet screening for depression and non-adherence is not a current standard of practice in this population. This study aimed to evaluate the association between depression and ARV adherence, and to investigate the effect of a brief screening intervention on these outcomes.

Methods: This prospective pre-post test study was conducted at an ambulatory HIV clinic in Windsor, Ontario. Ninety-four patients presenting during the study period consented to completing two validated self-administered questionnaires: the 10-item CES-D, evaluating depressive symptoms, and the SMAQ, evaluating ARV non-adherence. Clinic professionals were alerted when patients screened positively on either tool, with no directions for subsequent patient management. Approximately four months later, all 94 patients were contacted for a follow-up screening. Logistic regression was used to investigate the association between depressive symptoms and ARV adherence. Pearson's Chi Square was used to evaluate any differences in depression and adherence before and after the screening intervention.

Results: Depression was not associated with ARV non-adherence at either screen. On the first screen, female sex was found to be associated with ARV non-adherence ($p=0.04$), but this modest effect was not present at follow-up. There was no difference in rates of self-reported depression between the two screens ($p>0.2$). The proportion of patients screening positively for ARV non-adherence was 45.7% at the first screen and 27.8% at the second screen ($p<0.02$). Fifteen patients were lost to follow-up.

Conclusion: This study did not find adherence to be negatively correlated with depression. Statistically higher rates of adherence were reported after the brief screening intervention. Brief screening may in fact improve ARV adherence. Larger studies of longer duration would be needed to confirm these findings.

CSP1.05

Factors affecting adherence to Antiretroviral Therapy Among School Going Adolescents in Uganda

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Background: The scale up of ART treatment in Uganda has contributed to a number of children growing unto adolescents and living longer however faced with different ART challenges that impede adherence to ART. Limited information is known concerning adherence to ART and barriers to adherence among school going adolescents in Uganda.

Methodology: The study was cross sectional, conducted in 2011, 2012 at Mbarara Regional Hospital, used both qualitative and quantitative methods. Enrolled 102 adolescents, 13 to 20 years old, and 3months on ART. Data was collected using questionnaires, 6 focus group discussions and 10 key informant interviews. Subjects consented or assented. Permission was obtained from their guardians. Adherence was measured using a 30-day visual analogue scale.

Result: Of the 102 participants, 39.3% males, 60.8% were females, 70% were adhering to ART, mean adherence was 90% with (95% CI: 86.00-93.99). Fear of disclosure of HIV status was 49% stigma 77.2% reported as major challenges to ART adherence. Qualitative findings revealed that mostly competitive demands like meeting clinic appointment for care and drug refill and attending school activities, fear of disclosure of HIV status, Stigma and lack of food and safe drinking water impede adherence to ART among school going adolescents.

Conclusion: 30% of adolescents do not adhere to ART, Interventions are needed to build social support systems, set up linkages of HIV programs to existing child/ adolescents protection programs to enhance access to care, treatment, retention to ART, reduce stigma and promote disclosure.

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

Timing and Type of Maternal Combination Antiretroviral Therapy during Pregnancy Affects Placental Telomeres and Mitochondrial DNA Content

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Background: Combination antiretroviral therapy (cART) has been reported to affect leukocyte telomere length (TL) and mitochondrial DNA (mtDNA) content. Increased risks of preterm delivery have been reported in HIV+ women, with studies suggesting an association with exposure to antiretroviral drugs, some of which can cross the placenta. Our objective was to measure TL and mtDNA content in

placental tissue from HIV+ women, and investigate associations between these markers of cellular health and cART-related factors.

Methods: HIV+ pregnant women were enrolled in two prospective cohort studies. Placental tissue DNA was extracted from both the fetal (F) and maternal (M) sides of the organ, and TL and mtDNA content were measured by qPCR. Univariate associations were investigated by Student's t-test, Mann-Whitney or Fisher's test, and important factors ($p<0.15$) considered while developing multivariable models.

Results: Placenta tissue was obtained from 58 participants aged 21-45y, of whom 12 had a preterm delivery (< 37w gestation) and 20 conceived while on cART. The most common cART regimens in pregnancy were AZT+3TC+LPV/r (n=24) and AZT+3TC+NFV (n=15). In multivariable linear regression analyses of TL that included age, preterm delivery, cART type (LPV/r *vs.* NFV *vs.* other), and infant sex, shorter placental TL was independently associated with LPV/r treatment ($p\leq0.031$). Shorter placental TL (M) was also associated with preterm delivery ($p=0.033$). For mtDNA, in a model that included age, cART type and timing of cART initiation (pre- *vs.* post-conception), lower placenta mtDNA (F) content was independently associated with having conceived on cART ($p=0.033$). Lower placental mtDNA (M) was seen in women who received LPV/r ($p=0.025$) and a weak association was present in those who conceived on cART ($p=0.065$).

Conclusions: These results suggest that LPV/r-based regimen may modulate placental telomeres and mtDNA differently than the ritonavir-sparing NFV-based regimen. These markers could in turn reflect differences in placental development/function.

CSP2.02

Switching Tenofovir DF to Tenofovir Alafenamide in Virologically Suppressed Adults

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Background: Tenofovir alafenamide (TAF) is a novel nucleoside reverse transcriptase inhibitor (NRTI) that achieves 91% lower plasma tenofovir levels than TDF. In elvitegravir/cobicistat/F/TAF phase 3 studies, TAF had less adverse effect on kidneys and bone than TDF.

Methods: We conducted a 96-week (wk) randomized, double blind, active controlled study in virologically suppressed HIV-1 infected patients receiving F/TDF-containing regimens to evaluate the efficacy and safety of switching from F/TDF to F/TAF vs continuing F/TDF while remaining on the same third agent. Primary endpoint was virologic success at Wk 48 by ITT FDA snapshot algorithm with a pre-specified noninferiority margin of 10%. We describe the Wk 48 data.

Results: 663 patients were enrolled (F/TAF 333 vs F/TDF 330); median age 49 years, 15% women, median estimated glomerular filtration rate (eGFR) 100 mL/min. 46% were on a boosted protease inhibitor, 28% on an integrase inhibitor, 25% on a non-NRTI. Through week 48 switching to F/TAF was non-inferior to remaining on F/TDF (94.3% vs 93%; difference +1.3%, 95% CI: -2.5% to +5.1%). Emergent resistance was rare (0.3% vs 0). Drug related serious adverse events were rare (0 vs 0.3%). Drug discontinuation due to adverse events was low (2.1% vs 0.9%). There were no cases of proximal renal tubulopathy. Median eGFR improved by +8.4 mL/min with F/TAF vs +2.8 mL/ min with F/TDF ($P<0.001$). Quantitative measures of proteinuria improved with F/TAF but not with F/TDF. Bone mineral density increased with F/TAF but declined with F/TDF: hip (mean) +1.14% vs -0.15% ($P<0.001$) and spine +1.53% vs -0.21% ($P<0.001$), respectively.

Conclusions: In virologically suppressed patients switching from F/TDF to F/TAF, high rates of virologic suppression were maintained, while renal and bone safety parameters improved suggesting F/TAF has the potential to become an important NRTI backbone for antiretroviral treatment.

CSP2.03

Switching to Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (E/C/F/TAF) plus Darunavir (DRV) in Treatment-Experienced HIV-1 infected Adults

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Background: Strategic simplification of an antiretroviral regimen with high pill burden and dosing frequency is a priority for treatment-experienced patients with multidrug resistance This study evaluated the efficacy and safety of switching to E/C/F/TAF +DRV in patients with ≥ 2-class resistance, including TDF resistance mutations (K65R, ≤3 TAMs).

Methods: Virologically suppressed adults (N=135) on a DRV-containing regimen for ≥ 4months, with two prior failed regimens, and no history of Q151M, T69ins, or DRV RAMs, were randomized 2:1 to open-label E/C/F/TAF +DRV or to continue baseline regimen (BR). Week (W) 24 viral suppression (HIV-1 RNA <50c/mL) by FDA snapshot analysis and safety data are reported.

Results: Participants were older (median age 49), 25% female, 45% black, and 14% Hispanic. At entry, the median pills/regimen was 5, with 65% taking a twice-daily regimen, and a majority (58%) on a TDF-containing regimen. Viral suppression was maintained in 96.6% (86/89) in the E/C/F/TAF +DRV arm and 91.3% (42/46) in the BR arm (95%CI: -3.4%, 17.4%). There was no emergence of resistance. There were no differences in the median change in eGFR [2.5 in the E/C/F/TAF+DRV vs. -0.1mL/min in the BR arm (p=0.62)] or urine protein/creatinine (Cr) ratio [-14% in the E/C/F/TAF +DRV arm vs. -4% in BR arm (p=0.21)]. Specific markers of proximal tubular proteinuria improved with E/C/F/TAF +DRV: median urine beta-2M/Cr decreased 35% (p<.001) and median urine RBP/Cr decreased 17% (p=.019), compared to increases of 11% and 13% respectively in the BR arm. There were no drug-related SAEs and no AEs leading to treatment discontinuation.

Conclusions: Through W24, strategic simplification to E/C/F/TAF + DRV (two pills once daily) maintained viral suppression, and the switch to TAF was associated with significant improvement in proximal tubular proteinuria. E/C/F/TAF +DRV may offer an attractive option for treatment-experienced patients on complex multi-tablet regimens.

CSP2.04

A Prospective Pilot Study of Treatment Simplification to elvitegravir/cobicistat/emtricitabine/tenofovir DF (E/C/F/TDF) plus darunavir

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Objectives: To assess safety, efficacy, and pharmacokinetics of regimen simplification to E/C/F/TDF plus darunavir 800mg once daily, among HIV-infected adults receiving a complex multidrug regimen.

Methods: The study enrolled HIV positive adults with plasma viral load (VL) <40 copies/mL at screening and consistently <200 copies/mL for ≥ 6 months while receiving raltegravir or dolutegravir, ritonavir-boosted atazanavir or darunavir, and 2 NRTIs. Pre-dose darunavir levels were measured using a validated LC-MS/MS method at baseline and again ≥2 weeks after starting E/C/F/TDF + darunavir. Clinical and laboratory assessments were planned at weeks 2, 12, 24, 36, and 48.

Results: Nine participants were enrolled between October 2014 and October 2015. Baseline CD4 counts were 70-900 (median 440) cells/mm^3. Pre-switch regImens included tenofovir DF/emtricitabine (n=9), raltegravir twice daily (n=8), dolutegravir once daily (n=1), darunavir/ritonavir 800mg/100mg once daily (n=6), darunavir/ritonavir 600mg/100mg twice daily (n=1), and atazanavir/ritonavir once daily (n=2). Despite generally low darunavir trough levels (see Table), all 8 participants who have completed 12 weeks and all 5 who have reached 48 weeks have maintained VL <40 copies/mL. Subject 3 had proteinuria (UACR 19.2 mg/mmol) and hypophosphatemia (0.66 mmol/L) with eGFR 62 at baseline; at week 48, corresponding values were UACR 11.2 mg/mmol, phosphate 0.99 mmol/L, eGFR 50. No significant clinical or laboratory adverse events have been observed.

Conclusion: Despite low plasma darunavir concentrations, treatment simplification to a two-pill once daily regimen of E/C/F/TDF + darunavir has been safe and effective thus far for nine HIV+ patients who were previously stable on multidrug antiretroviral regimens.

Subject	Gender	Age, years	Weight, kg	Plasma darunavir, ng/mL		
				Baseline, pre-dose	On-study pre-dose	On-study 24 hours post-dose
1	M	59	92.5	1150	1030	254
2	M	47	89.5	667	198	-
3	M	71	63.0	-	643	322
4	M	55	101.5	802	391	753
5	F	42	56.0	-	456	336
6	M	33	85.5	-	-	-
7	M	53	72.0	-	1570	816
8	M	56	95.5	981	135	456
9	F	48	84.0	1060	601	586

CSP2.05

The Impact of the Composition of Physicians' Practices on Mortality

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Background: We examined mortality rates of HIV+ men and women who started highly active antiretroviral therapy (HAART) in British Columbia (BC), by selected characteristics of their follow-up physician.

Methods: HIV+ patients, aged ≥19 years, who initiated HAART between 01/ 2000 and 12/2013, with a known follow-up physician, who were actively followed for at least one-year following HAART initiation were eligible for this study. The outcome was all-cause mortality, determined through linkages to the BC vital statistics registry. Independent variables examined included physician experience (i.e. number of patients receiving antiretrovirals (ARVs) who were previously cared for; unit per 10% increase), the proportion of clients in the physician's practice from selected transmission and ethnic groups, and health authority of the practice.

Results: 4,447 HIV+ adults were eligible for our study. Patients were seen by 684 follow-up physicians with a median physician experience of 136 (Q1-Q3: 33-320) HIV+ persons ever on ARVs. In multivariable survival analysis, patients with follow-up physicians who provided care to a higher proportion of patients with injection drug use history (AHR = 1.13, 95% CI:1.09-1.17), Indigenous ancestry (AHR = 1.06, 95% CI: 1.02-1.10) and who cared for a majority of patients from health authorities outside Vancouver Coastal (AHR = 1.27, 95% CI:1.05-1.53), were at increased risk of death over the follow-up period.

Conclusions: We found that patients treated by follow-up physicians who provided care to a more marginalized population had higher rates of mortality. This association was independent of physicians' previous experience in treating patients on ARVs

CSP2.06

Integrase Inhibitor-Based Antiretroviral Therapy in Vulnerable Populations

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Background: Current treatment guidelines favor the use of integrase inhibitor (II) based regimens in the majority of settings where antiretroviral therapy (ARV) is required, based on the results of clinical trials demonstrating the superiority of such approaches. Vulnerable inner-city populations have not been evaluated in such trials. There is a need to generate data in such populations to validate the generalizability of treatment guidelines in these populations.

Methods: We have conducted a retrospective analysis of the database of a large clinic catering to HIV-infected patients with a high prevalence of recreational drug use. We have abstracted records of subjects receiving II-based therapy, based on the ability to achieve and maintain virologic suppression. Demographic and clinical correlates of success were evaluated, with a view to comparing the relative efficacy of raltegravir (RAL), elvitegravir (ELV) and dolutegravir (DOL)-based regimens.

Results: A total of 247 patients received IIs (141 RAL, 68 ELV, 38 DOL). Baseline characteristics include: 85.8% male, 38.5 % intravenous drug users, 5.3% naïve before this ARV regimen, 45.2 % HCV co-infected, and 13.6 % on opiate substitution therapy. Median baseline CD4 count and plasma viral load were 410 (Range:30-1380) cells/mm^3 and 43 (Range:<40-300 000) copies/mL. After a median follow up of 44 (3-1412) months, virologic suppression was achieved in 93.0%/86.7%/97.3% patients on RAL/ELV/DOL with most current median CD4 count of 555 (Range:60-1700) cells/mm^3. No treatment-limiting toxicity was observed.

Conclusion: II-based therapies are as effective in "real life" as they have been reported to be in clinical trials, justifying their selection as regimens of choice for all patients. Medium and long-term efficacy of all 3 agents in this class are comparable, and the selection of one agent over another should be based on other criteria than virologic potency and tolerability.

CSP2.07

Privacy-Preserving Genomic Testing in the Clinic – a Model Using HIV Treatment

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Introduction: The implementation of genomic-based medicine is hindered by unresolved questions regarding data privacy and delivery of interpreted results to health care practitioners. We used DNA-based prediction of HIV-related outcomes as a model to explore critical issues in clinical genomics.

Methods: We genotyped 4149 markers in HIV+ individuals. Variants allowed for prediction of 17 traits relevant to HIV medical care, inference of patient ancestry and imputation of HLA types. Genetic data were processed under a privacy-preserving framework using homomorphic encryption, and clinical reports describing potentially actionable results were delivered to healthcare providers.

Results: A total of 230 patients were included in the study. We demonstrated the feasibility of encrypting a large number of genetic markers, inferring patient ancestry, computing monogenic and polygenic trait risks, and reporting results under privacy preserving conditions. The average execution time of a multi-marker test on encrypted data was 865 milliseconds on a standard computer. The proportion of tests returning potentially actionable genetic results ranged from 0-54%.

Conclusions: The model of implementation presented herein informs on strategies to deliver genomic test results for clinical care. Data encryption to ensure privacy helps build patient trust, a key requirement on the road to genomic-based medicine.

CSP2.08

Persistent CD8 T-cell elevation: Contribution of Microbial Translocation, Inflammation and ART following Primary HIV-1 Infection

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Introduction: CD4 T cell depletion and chronic immune activation are the hallmark of HIV infection. Recently CD8 T cell elevation has been independently linked with non-AIDS events even in long-term chronically ART treated patients. We have previously shown the contribution of early initiation of ART on reduction of CD8 T cell counts. Here, we assessed the association of microbial translocation and inflammatory cytokines with CD8 T cell elevation in HIV patients during early infection.

Methods: We prospectively assessed 45 individuals who participated in the Montreal Primary HIV Infection (PHI) Study with an estimated date of HIV acquisition of less than 180 days, and compared with 11 elite controllers (ECs) and 11 uninfected controls. Influence of patient characteristics, markers of microbial translocation (LPS, sCD14) and inflammation (IFN-γ, IL-6, IL-18) was assessed as a potential contributing factor to the elevation of CD8 T cells.

Results: Median CD8 T cell counts were significantly elevated during untreated PHI vs controls (800 vs 425 cells/uL, p<0.001) and persisted over time (750 cells/uL, p=0.002). ECs presented with less elevated counts and higher than the controls (720 cells/uL). Early ART initiation decreased the CD8 counts without normalization. CD8 counts correlated positively with CD4 counts (r=0.474, p=0.001), negatively with CD4/CD8 ratio (r=-0.603, p<0.001) and were not influenced by viral load and LPS (p>0.05). Positive correlation of CD8 counts was observed with sCD14 (r=0.298, p=0.047), IFN-γ (r=0.426, p=0.024), IL-6 (r=0.386, p=0.008) and IL-18 (r=0.338, p=0.023).

Conclusions: CD8 T cell elevation persists despite early ART and is associated with markers of microbial translocation and inflammation and may contribute to the better understanding of mechanistic links related to non-AIDS events. CD8 T cell count can be used as an easily available marker for persistent level of immune activation and inflammation.

CSP2.09

Predictors of Viral Suppression and Rebound among HIV-Positive Men who have Sex with Men in a Large Multi-Site Canadian Cohort

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Objectives: Gay, bisexual and other men who have sex with men (MSM) are disproportionately affected by HIV in Canada. Combination antiretroviral therapy (cART) dramatically decreases progression to AIDS, premature death and HIV transmission. However, there are no comprehensive data regarding cART outcomes among MSM in Canada. We sought to identify socio-demographic and clinical correlates of viral suppression and rebound.

Methods: Our analysis included MSM participants in the Canadian Observational Cohort (CANOC) collaboration, aged ≥ 18 years who first initiated ART between 2000 and 2011. We used multivariable accelerated failure time models to identify factors predicting time to suppression (2 measures < 50 copies/mL ≥ 30 days apart) and subsequent rebound (2 measures > 200 copies/mL ≥ 30 days apart).

Results: Of 2,858 participants identified as MSM, 2,448 (86%) achieved viral suppression in a median time of 5 months (Q1-Q3:3-7 months). Multivariable analysis identified later calendar year of ART initiation (adjusted hazard ratio [aHR]=1.26, 95% CI:1.11-1.42 for 2004-07, aHR=1.32, 95% CI:1.17-1.48 for 2008-12 relative to 2000-03), and older age (aHR 1.08 per 10 year increment, 95% CI:1.03-1.13) as predictors of viral suppression. Injection drug use (IDU) history (aHR 1.41, 95% CI:1.18-1.67), higher baseline viral load (aHR 0.73 per log10, 95% CI:0.66-0.80), and being on an initial regimen consisting of boosted PIs (aHR 0.81, 95% CI:0.74-0.90) or unboosted PIs (aHR 0.60, 95% CI:0.48-0.76) relative to NNRTIs predicted lower likelihood of suppression. Among those who suppressed, 295 (12%) experienced viral rebound in a median time of 22 months (Q1-Q3:11-39 months). Significant (p < 0.05) predictors of rebound included earlier calendar year of ART initiation, IDU history, younger age, and higher baseline CD4 cell count.

Conclusion: Further strategies are required to optimize cART outcomes in MSM in Canada, specifically targeting younger MSM and those with a history of IDU.

Co-infections (including HCV, HBV, HPV, Syphilis, TB)
Coinfections (y compris VHC, VHB, papillomavirus, syphilis, tuberculose)

CSP3.01

Determining Hepatitis C Treatment Eligibility in a HIV/HCV Co-infected Northern B.C. Population: a Cross-sectional Chart Review

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HCV is a leading cause of mortality in the HIV-positive population, surpassing HIV itself. Within Northern B.C. it is estimated that co-infection rates may be as high as 60% due to shared routes of transmission. In recent years treatment options for HCV have dramatically improved with the development of direct acting antivirals (DAAs) that are more efficacious and better tolerated compared to traditional interferon-based therapies.

Our aim is to determine the number of HIV/HCV co-infected patients who are clinically eligible for HCV treatment as well as provincial drug coverage. Secondary endpoints include the frequency of HCV genotypes, vaccination status and perceived barriers to treatment.

This retrospective cross-sectional chart review included all HIV/HCV co-infected patients in Northern B.C. Clinical eligibility for HCV treatment was dependent upon absence of treatment contraindications. Drug coverage eligibility was determined by meeting current B.C. PharmaCare special authorization criteria. Barriers to treatment include drug interactions between HCV and HIV therapies that require a change in HIV therapy or increased monitoring, caution with a co-morbidity, social barriers and drug coverage.

Initially, 129 HIV/HCV co-infected patients were identified for review. Most common reason for exclusion were negative HCV RNA (n=17) and moved or not seen in greater than 5 years (n=36). Seventy charts were included in the study. Of those, 69 (99%) were determined to be clinically eligible for at least one of the indicated treatment options. Coverage eligibility was more limited with only 27 (39%) patients qualifying, largely due to few patients with significant enough fibrosis (Metavir ≥F2).

We have identified a large gap between clinical and provincial eligibility for HCV treatment among our HIV/HCV co-infected population in Northern B.C. Realistically, patients who are not eligible for PharmaCare coverage will not be treated unless they have other drug coverage; leaving drug cost as the largest barrier to treatment.

CSP3.03

Ledipasvir/Sofosbuvir is Safe and Effective for the Treatment of Patients with Genotype 1 Chronic HCV Infection in Both HCV Mono-and HCV/HIV Co-infected Patients

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Background: Current guidelines state that HCV/HIV-coinfected persons should be treated same as persons without HIV. We compared safety and efficacy of ledipasvir/sofosbuvir (LDV/SOF) in HCV/HIV GT1 patients in the Phase3 ION-4 study with HCV monoinfected GT1 patients in the Phase3 ION 1-3 studies.

Methods: In the ION-4 study, 327 GT1 HCV/HIV patients received LDV/SOF 90/400 mg daily for 12 weeks. In the ION 1-3 studies, 538 GT1 HCV mono patients received LDV/SOF for 12 wks. This pooled analysis will assess safety and SVR12. LDV, SOF and GS-331007 exposures in HCV/HIV subjects were compared across ARVs , race, SVR12, and to subjects with HCV monoinfection. A genome-wide association study (GWAS) was conducted to identify host genetic determinants of HCV relapse after LDV/SOF in HCV/HIV individuals on ARVs.

Results: 865 patients were treated with 12 weeks of LDV/SOF in the Phase3 ION program. In ION-4, the overall SVR12 was 96% and relapse was 3%. In ION 1-3, overall SVR12 was 97% and relapse was 2%. SVR12 by treatment history, cirrhosis status, race and GT1 subtype are reported Table 1. Most common AEs (>10% reported in any arm) were fatigue, headache, diarrhea, and nausea. There were no clinically relevant differences in PKof LDV/SOF in HCV/HIV subjects compared to HCV mono subjects. The GWAS did not reveal significant associations with HCV relapse.

Conclusions: In this analysis, LDV/SOF for 12 wks provided high rates of SVR regardless of HIV infection and is a safe, well-tolerated option for patients with both HCV mono-infection and HCV/HIV co-infection

TABLE 1. SVR12 by treatment history, cirrhosis status, race and GT 1 subtype.

Study	ION 1	ION 2	ION 3	ION 1-3 Combined	ION 4 (HIV)
Treatment Naïve SVR12 (%)	210/213 (99)		208/216 (96)	418/429 (97)	138/146 (95)
Treatment Experienced SVR12 (%)		102/109 (94)		102/109 (94)	175/181 (97)
Cirrhosis SVR12 (%)	32/34 (94)	19/22 (86)		51/56 (92)	63/67 (94)
Noncirrhotic SVR12 (%)	179/179 (100)	83/87 (95)	208/216 (96)	470/482 (98)	250/260 (96)
Blacks SVR12 (%)	24/24 (100)	24/24 (100)	40/42 (95)	89/90 (99)	103/115 (90)
Nonblacks SVR12 (%)	188/190 (99)	78/85 (92)	165/173 (95)	431/448 (96)	215/217 (99)
GT 1a	142/145 (98)	82/86 (95)	165/172 (96)	389/403 (97)	239/250 (96)
GT 1b	67/67 (100)	20/23 (87)	43/44 (98)	130/134 (97)	74/77 (96)

CSP3.04

Risk Factors for Oncogenic, High-Risk Human Papillomavirus Infection of the Anal Canal in Men Who Have Sex With Men (MSM)

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Background: Infection with high-risk human papillomavirus (HR-HPV) is a necessary step in the carcinogenesis of anal squamous cell carcinoma (SCC). Anal SCC is a malignancy disproportionately affecting MSM, particularly HIV-positive individuals. Despite this, there is limited evidence for specific sexual and behavioural HR-HPV risk factors in this population.

Methods: A cross-sectional study recruited a clinic-based sample of HIV-positive and HIV-negative MSM. Participants completed a sociobehavioural questionnaire and sexually transmitted infection testing, including anal swabs for HPV-DNA testing. A Luminex-based HPV assay detecting 46 types, including 13 HR-HPV types, was used. Multivariable logistic regression was performed to assess risk factors associated with HR-HPV infection.

Results: 429 MSM were recruited: 267 HR-HPV-positive and 162 HR-HPV-negative. Median age was 45 (IQR=22-72) and 46 years (IQR=23-70), respectively. Multivariable logistic regression revealed risk factors associated with HR-HPV infection in the overall population: HIV positivity (OR: 1.86; 95%CI 1.20-2.89); current smoker (OR: 2.24; 95%CI 1.33-3.79); and, ≥ 50 lifetime sexual partners (OR: 2.37; 95%CI 1.05-5.35). Number of recent (i.e. previous six months) sexual partners was not associated with HR-HPV infection (OR: 1.24; 95%CI 0.76-2.02). Current smoking status remained a risk factor for HR-HPV infection in separate analyses of the HIV-positive (OR: 2.11; 95%CI 1.09-4.12) and HIV-negative (OR: 2.30; 95%CI 1.02-5.34) populations.

Conclusions: The study highlights the importance of HIV serostatus, smoking, and number of sexual partners as significant predictors of HR-HPV anal infection, an important precursor to anal SCC. It further clarifies the likely role played by sexual behaviours in HPV acquisition, and the likely contribution of smoking to HPV persistence, signalling that smoking cessation as an intervention in certain populations may lower the risk for persistent HR-HPV infection, along with other health benefits for men. There remains a need for evidence-based screening, diagnostic and treatment strategies for anal dysplasia and anal cancer prevention among MSM.

CSP3.05

HCV Treatment of HIV-HCV Co-Infected PWID at a Tertiary Clinic

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Background: People who inject drugs (PWID) are overrepresented among HIV-HCV co-infected adults. HCV treatment regimens are equally effective in the setting of HIV co-infection. However, the feasibility and success of such therapy has not yet been studied. The aim of this analysis was to address this knowledge gap.

Methods: Our goal was to identify, recruit, and retain HCV co-infected PWID in care. We established a multidisciplinary program including access to specialty medical care, support services, comprehensive management of social needs, and addiction treatment. We have conducted a retrospective analysis of all HIV co-infected patients treated for HCV at our centre. This analysis correlates the likelihood of achieving sustained virologic response (SVR) following HCV treatment with a range of baseline demographic and clinical variables.

Results: Of 522 HIV-infected, 247 (47.3%) were co-infected with HCV. Among the latter, 167 (67.6%) were PWID and 77 (31.2%) have completed HCV treatment (72 interferon-based, 5 all-oral regimens), 46 (59.7%) had genotype 1 infection. The mean age was 51, 70 (90.9%) were male, 24 (31.2%) were on opiate substitution, 73 (94.8%) were on HIV treatment (62/73 with full virologic suppression), 21 (27.3%) were homeless, and 33 (42.9%) attended weekly HCV support groups. The SVR rate was 46.8% (36/77), 3/5 (60%) on all-oral regimens, 21/46 (45.7%) with genotype 1, and 3/3 (100%) for patients with genotype 1 on all-oral regimens. Success rates were higher in subjects on meth-

adone at 16/24 (66.7%), and no lower in those who were homeless 11/21 (52.4%) or active PWID 26/54 (48.1%).

Conclusions: PWID with HIV co-infection can be successfully treated for HCV infection within multi-disciplinary programs. Such programs will serve as an important tool to address the HCV epidemics in vulnerable populations considered as "core transmitters" of HCV and HIV, especially as highly effective all-oral regimens become the standard of care.

CSP3.06

Real world outcomes with hepatitis C direct acting antiviral agents are similar to those achieved in clinical trials in HIV/HCV co-infected patients

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Outcomes of direct acting antiviral therapy (DAA) in co-infected patients treated in a real world setting are not well established. We undertook an analysis of outcomes of individuals undertaking HCV therapy at a hospital-based co-infection clinic in British Columbia.

Data were analyzed from the St Paul's co-infection clinic from January 2005 to December 2015. Therapy included use of combination pegylated interferon/ribavirin (PR) with DAA, or interferon-free DAA therapy following standard algorithms. Participants were recorded as achieving an end of treatment response (EOT) if HCV RNA was undetectable at end of therapy, and SVR 12/24. Factors associated with treatment initiation were analyzed using logistic regression models adjusted for age, gender, IDU status, calendar year of initial assessment and evidence of cirrhosis.

Overall 329 individuals were assessed for HCV therapy (85% male, 46% IDU, median (q1-q3) age at baseline 47(42-53), and 238 individuals initiated therapy. For (n =170,71%) genotype 1/4 individuals 84(49%) received DAA therapy and 57(34%) received interferon-free DAAs. For (n = 71, 30%) genotype 2/3 individuals, 10(14%) received DAA based therapy. SVR rates are displayed in Table 1. SVR was achieved by 95% of those treated with PR-DAA and 92% of those treated with interferon-free DAAs. Factors associated with treatment initiation including being MSM(adjusted odds ratio [aOR]: 3.09(95% CI 1.01-9.46), year of first HCV visit: 2008-2012 vs.2003-2007 (aOR: 11.32(4.52-28.36), 2013-2015 vs.2003-2007 (aOR: 10.53(4.03-27.50), and having evidence of cirrhosis (aOR: 8.94(3.32-24.11).

Outcomes attained using DAA therapies are high (> 95%) and are similar to those seen in the clinical trial setting.

Table 1. Outcomes of HIV/HCV co-infected patients initiating DAA therapy.

Genotype	Initiated Therapy	Regimen	End of Treatment Response (% of those who reached time point)	SVR 12/24 (% of those who have reached time point)
1/4	27	PR- telaprevir/ boceprevir/simeprevir/sofosbuvir	22 (100%)	18 (95%)
	57	Interferon-free DAA:s	48 (98%)	12 (92%)
	52	Sofosbuvir/Ledipasvir		
	2	Sofosbuvir/Ledipasvir/Ribavirin		
	2	Simeprevir/Sofosbuvir/Ribavirin		
	1	Simeprevir/Sofosbuvir		
2	3	Sofosbuvir/ribavirin	1 (100%)	1 (100%)
3	7	Sofosbuvir/ribavirin	4 (100%)	--------

CSP3.07

Sampling for Herpesvirus Reactivations in Hospitalized HIV+ Adults: a Pilot Study

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Background: Asymptomatic reactivations of cytomegalovirus (CMV) and herpes simplex virus type 2 (HSV2) are associated with worse clinical outcomes in critically ill non-HIV infected patients, but their impact among hospitalized HIV+ individuals is unknown. To plan for future studies addressing this question, we assessed feasibility of collecting serial mucosal and blood specimens in this setting.

Methods: HIV+ adults admitted to St. Michael's Hospital with acute illnesses unrelated to HSV/CMV were approached. Consenting patients underwent chart review, and baseline HSV2 and CMV serologic testing if serostatus was unknown. Mucosal swabs (oral, genital, anal) and plasma were collected thrice weekly for HSV2 and CMV PCR for up to six visits. Interim findings are summarized using descriptive statistics.

Results: 45/81 (55.6%) of inpatients approached consented to participation. Common reasons for refusal were: lack of interest (n=15), stress from other medical illnesses (n=8), recent HIV diagnosis (n=2), and concern about risks (n=2). Reasons for hospital admission were AIDS-defining illnesses (n=16), acute non-HIV-related illnesses (n=27) and exacerbations of chronic conditions (n=2). Median (IQR) age was 47 (41, 51) years, CD4 count=127 (40,334) cells/mL, and viral load=574 (39,16086) copies/mL. Most participants were male (88.9%, 40/45). Most common HIV risk

factors were MSM (55.6%, 25/45), endemic country (13.3%, 6/45), and MSM-IDU (11.1%, 5/45). Coinfection was common at 64.4% (29/45) for HSV-2 and 88.9% (40/45) for CMV; only one participant was seronegative for both viruses. Both mucosal swabs and blood sampling was possible for 86.7% of participants (39/45); another 4.4% (2/45) have swabs only and 4.4% (2/45) have blood only. PCR testing of collected specimens is pending. Median (IQR) hospital length of stay was 8 (6, 18.5) days.

Conclusions: High prevalence of coinfection and >50% consent for serial specimen collection in this setting suggest that further work assessing the relationship between herpesvirus reactivations and clinical outcomes is feasible.

CSP3.09

HCV Direct Acting Antivirals (DAA) are Metabolically Safe and Highly Curative Irrespective of HIV Status

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Introduction: Historically, HCV treatment outcomes have been poor in HIV-HCV co-infection compared to HCV mono-infection. Recent evidence suggests that this efficacy and safety gap has been closed with DAAs.

Methods: DAA recipients were identified from The Ottawa Hospital and Regional Viral Hepatitis Program Database. Baseline characteristics were identified; on-treatment virological, enzymatic and metabolic responses determined; and sustained virological response (SVR) assessed and compared between HIV-HCV and HCV.

Results: Aside from gender, baseline characteristics were similar (Table). Enzymatic suppression was robust and similar between groups. Glucose and lactate levels remained unchanged on-treatment. SVR in genotype 1 was high, irrespective of HIV status.

Discussion: SVR is much improved with DAA treatment and the SVR gap in HIV co-infection has been bridged. DAA metabolic toxicities were not identified.

	HCV Patients			
	HIV+	**HIV-**	**Total**	**p-value**
	n=13 (7.7%)	n=155 (92.3%)	n=168 (100%)	
Age (mean)	56.4	53.8	56.2	0.33
Male Sex (%)	92.3	60.7	63.1	0.02
White/Black/Asian/ Indigenous (n)	8/3/0/0	113/10/7/3	121/13/7/3	0.145
Genotype 1/2/3/4 (n)	7/1/1/4	123/9/21/2	130/10/22/6	<0.001
Cirrhosis (%)	50.0	44.7	45.1	0.722
DAA Treatment Regime				0.724
LDV+SOF	46.2	41.9	42.3	
LDV+SOF +RBV	7.7	9.0	8.9	
SMV+SOF	7.7	6.5	6.6	
SOF±SMV +RBV	30.8	40.7	39.9	
Other DAA +RBV	7.7	1.9	2.4	
Baseline ALT (U/L)	77.0	99.1	97.4	0.330
End of Treatment ALT	44.2	36.3	36.9	0.443
ΔALT	-29.4	-61.8	-59.4	0.129
Baseline Lactate (mmol/L)	2.6	2.4	2.5	0.564
End of Treatment Lactate	1.7	2.2	2.2	0.179
ΔLactate	-1.2	-0.4	-0.5	0.009
Baseline Random Glucose (mmol/L)	5.9	6.3	6.2	0.721
End of Treatment Glucose	6.2	6.0	6.0	0.840
ΔGlucose	0.3	-0.3	-0.3	0.543
SVR (All) (%)	75.0 (n=12)	91.1 (n=123)	89.6 (n=135)	0.083
SVR (Genotype 1) (%)	100.0 (n=6)	96.04 (n=97)	96.3 (n=103)	0.619
SVR (Genotype 3) (%)	0.0 (n=1)	53.9 (n=13)	50.0 (n=14)	0.299

CSP3.10

Hepatitis B Vaccination Response Rates in Canadian Pediatric Patients Living with HIV

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Objectives: Children living with HIV receive double dose of monovalent vaccine (Recombivax 10ug or Engerix 20 ug) per Canadian guidelines. This retrospective chart review was conducted to review HBV vaccine administration practices, and evaluate response rates at our centre.

Methods: Medical records of patients in the pediatric HIV clinic at SickKids from 1995 to 2014 were reviewed. Patients were excluded if they received <3 doses of vaccine or had no post-vaccination titers performed.

Results: Of 71 patients reviewed, 50 met the inclusion criteria (17 excluded for having received <3 doses, 4 for lacking antibody titer testing). Median age of the 50 subjects at the time of completion of the three-dose series was 11 years (IQR 6,13); 46% were male. Median CD4 count at the time of vaccination was 894 cells/ul (IQR 703,1146), median viral load at the time of vaccination was 0 copies/mL (IQR 0, 39) and CD4 nadir was 421 cells/ul (IQR 294,605). Median BMI was 18 (IQR16, 21). Protective titres (median 112 IU/mL; IQR1, 644) were demonstrated in 66% (n=33) of subjects a median of 16.5 months after completion of the vaccine series. Of the remaining 17, 8% (n=4) had detectable, but non-protective (<10 IU/mL) anti-HBV titers and 26% (n=13) had no detectable responses. Of these 17 subjects, 4 received a second series of vaccine and showed protective responses. There were no significant correlations or

associations demonstrated on univariate analysis between protective anti-HBV titers and age at vaccination, gender, VL, CD4 count, CD4 count nadir or BMI.

Conclusions: In this single-centre cohort of children there was an overall low vaccine response rate (66%). No predictors of non-response were identified, possibly due to the small sample size and the retrospective nature of our study. The results suggest that a higher vaccine dose may be warranted for HIV-positive children.

CSP3.11

Viral Hepatitis Co-Infection and Chronic Kidney Disease Progression among HIV-Infected Canadians Initiating Antiretroviral Therapy

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Introduction: Hepatitis co-infection is prevalent in HIV and associated with extra-hepatic comorbidities. We investigated hepatitis B (HBV) and hepatitis C (HCV) virus co-infection and chronic kidney disease (CKD) progression among Canadians initiating antiretroviral therapy (ART).

Methodology: We included all patients in the Canadian Observational Cohort (CANOC) from 2000–2012 who had ≥ 3 creatinine measurements, including a baseline measurement ≤ 30 days prior to starting ART. Glomerular filtration (eGFR) was calculated using the CKD-EPI equation. CKD was defined as two eGFR measurements < 60 mL/min/1.73m^2 obtained ≥ 3 months apart. Patients with prevalent CKD were excluded. CKD incidence rates stratified by viral co-infection were calculated. Hazard ratios (HRs), adjusted for demographic variables, CD4$^+$ count, HIV viral load, initial ART regimen, baseline eGFR, hypertension, year of ART initiation, creatinine testing rates and competing risk of death, were estimated using the Fine and Gray model.

Results: 2,462 patients were followed for a total of 10,453 person-years (PYs). The median age at baseline was 40 (interquartile range: 33–46), 85% were male and 8% and 20% were co-infected with HBV and HCV, respectively. CKD incidence rates are presented in the Table. In multivariate analysis, HBV co-infection was not associated with CKD (HR 1.02; 95% confidence interval [CI]: 0.55–1.91), but HCV co-infection was associated with faster time to CKD (HR 2.00; 95% CI: 1.19–3.35).

Discussion: HCV, but not HBV co-infection, increased the risk of renal impairment independent of traditional chronic disease risk factors. Future research should explore the potential improvement of kidney function after HCV treatment.

Table: Crude CKD Incidence Rates (per 1,000 person-years)

	CKD Events	Person-Years	Incidence Rate	95% Confidence Interval
Overall	145	10,453.2	13.9	11.8, 16.3
HBV & HCV-HIV Co-Infected	5	174.9	28.6	11.9, 68.7
HCV-HIV Co-Infected	49	1,787.9	27.4	20.7, 36.3
HBV-HIV Co-Infected	6	614.5	9.8	4.4, 21.7
HIV Mono-Infected	85	7,875.9	10.8	8.7, 13.3

CSP3.12

Correlates of syphilis treatment success in a population with high rates of HIV co-infection in British Columbia

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Background: Syphilis is a common co-infection among people living with HIV (PLWH). In the context of increasing syphilis rates we sought to characterize the proportion of individuals who achieved treatment success and factors associated with success in British Columbia (BC).

Methods: Individuals with an infectious syphilis diagnosis, ≥2 RPR titre measurements between January 1, 1995 and December 31, 2010 and who received treatment were identified using provincial surveillance data. Treatment success was defined as A) a fourfold drop in titre within 12 months; and B) titre <1:8 within two years after diagnosis, as per the BC STI Treatment guidelines. We examined differences in treatment success by age, sex, exposure category, ethnicity, RPR titre at diagnosis, stage of infection, residence in the greater Vancouver area vs. outside, year of diagnosis, >1 syphilis diagnosis and HIV seropositivity. Multivariable logistic regression was performed to identify independent correlates of treatment success.

Results: Among 1741 individuals, there were 1959 syphilis diagnoses. 57.4% of cases achieved outcome A, 69.0% achieved outcome B and 46.9% achieved both outcomes. PLWH composed 33.5% of the cases and 46.6% were MSM. The median age was 38 years (IQR: 30-45). Cases among PLWH (adjusted OR(aOR): 1.60, 95%CI: 1.30-2.50); those residing in greater Vancouver (aOR: 1.25, 95% CI: 1.02-1.53); and those with RPR titres between 1:8-1:256 (aOR: 1.80, 95%CI: 1.41-2.29) and >1:256 (aOR: 1.83, 95%CI: 1.27-2.64) vs. <1:8 were more likely to achieve treatment success, while those diagnosed between 2000-2004 (aOR: 0.46, 95%CI: 0.32-0.66) and 2005-2010 (aOR: 0.43, 95%CI: 0.30-0.62) vs. 1995-1999 were less likely to achieve success.

Conclusion: Almost half of all syphilis cases in BC achieve treatment success based on a strict definition. PLWH are

more likely to achieve success. Further analysis is needed to differentiate treatment failure from re-infection.

CSP3.13

Drug-Drug Interactions Studies between HCV Antivirals Sofosbuvir and Velpatasvir and HIV Antiretrovirals (ARVs)

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Background: A sofosbuvir/velpatasvir (SOF/VEL) combination tablet is under regulatory review for HCV. Studies were conducted in healthy volunteers to evaluate potential drug-drug interactions (DDIs) between SOF/VEL and HIVARV regimens.

Methods: In multiple-dose, randomized, cross-over studies, subjects received SOF/VEL and EFV/FTC/TDF, RPV/FTC/TDF, DTG, RAL+FTC/TDF, EVG/COBI/FTC/TDF, DRV/r + FTC/TDF, ATV/r + FTC/TDF, LPV/r + FTC/TDF, or EVG/COBI/FTC/TAF alone and in combination. Steady-state plasma concentrations of SOF, its metabolite GS-331007, VEL, and ARVs were analyzed on the last day of dosing. PK parameters were calculated and geometric least-squares means ratios and 90% confidence intervals (combination vs. alone) for SOF, GS-331007, VEL, and ARV AUC_{tau}, C_{max} and C_{tau} were estimated and compared against lack of PK alteration boundaries of 70-143% for all analytes. Safety assessments were conducted throughout the study.

Results: 230 of 237 enrolled subjects completed the studies. The majority of adverse events (AEs) were Grade 1 and there were no serious AEs. Table 1 reports the effect of coadministration on HIV ARVs and SOF/VEL. No clinically significant changes in the PK of HIV ARVs, except TDF, were observed when administered with SOF/VEL. Increased TFV exposure (~40%) was observed when administered as TDF, but not as TAF.

Conclusions: Study treatments were generally well tolerated. Results from these studies demonstrate that SOF/VEL may be administered safely with RPV, RAL, DTG, EVG, COBI, DRV/r, ATV/r, and LPV/r but not EFV with a backbone of FTC/TDF or FTC/TAF. The safety and efficacy of SOF/VEL and ARVs are being evaluated in clinical studies of HIV/HCV coinfected patients.

Table 1. Effect of Coadministration on HIV ARVs and SOF/VEL

ARV with SOF/VEL	Effect on SOF/VEL AUC	Effect on ARV AUC
EFV/FTC/TDF	SOF: <-->	EFV: <-->
	GS-331007: <-->	FTC: <-->
	VEL: ↓53%*	TFV: ↑81%
FTC/RPV/TDF	SOF: <-->	FTC: <-->
	GS-331007: <-->	RPV: <-->
	VEL: <-->	TFV: ↑40%
DTG	SOF: <-->	DTG: <-->
	GS-331007: <-->	
	VEL: <-->	
RAL + FTC/TDF	SOF: <-->	RAL: <-->
	GS-331007: <-->	FTC: <-->
	VEL: <-->	TFV: ↑40%
DRV/r + FTC/TDF	SOF: ↓28%	DRV: <-->
	GS-331007: <-->	RTV: <-->
	VEL: <-->	FTC: <-->
		TFV: ↑40%
ATV/r + FTC/TDF	SOF: <-->	ATV: <-->
	GS-331007: <-->	RTV: <-->
	VEL: ↑142%	FTC: <-->
		TFV: <-->
LPV/r + FTC/TDF	SOF: ↓29%	LPV: <-->
	GS-331007: <-->	RTV: <-->
	VEL: <-->	FTC: <-->
		TFV: <-->
EVG/COBI/FTC/TDF	SOF: <-->	EVG: <-->
	GS-331007: <-->	COBI: <-->
	VEL: <-->	FTC: <-->
		TFV: <-->
EVG/COBI/FTC/TAF	SOF: ↑37%	EVG: <-->
	GS-331007: ↑48%	COBI: <-->
	VEL: ↑50%	FTC: <-->
		TAF: <-->
		TFV: <-->

* PK/Pharmacodynamic data from Phase 3 trials will guide recommendation for use of SOF/VEL with EFV-containing regimens.

CSP3.14

Improving Hepatitis C Care at an Indigenous focused urban-core clinic in Vancouver

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Background: Advances in Hepatitis C Virus (HCV) medications have eliminated many biomedical barriers, however, other healthcare and socioeconomic barriers still need to be addressed to increase linkage to care and treatment to prevent further HCV infection, associated liver morbidity, and mortality, in particular among those co-infected with HIV and Indigenous Peoples who are disproportionately affected in Canada.

The "HCV Care Cascade" tracks medical care and number of affected individuals among a particular population from screening to Sustained Virological Response (SVR). The baseline HCV Care Cascade at Vancouver Native Health Society (VNHS) Medical Clinic, in urban core Vancouver is as follows: of 2776 active patients (2013-2015), 1317 were screened for HCV, 782 were identified as ever exposed, 441 as chronically infected, 88 initiated treatment, 59 achieved treatment SVR; 177 were HCV/HIV co-infected.

Research Aims & Question: *Primary Research Question*: Can adopting a quality improvement Chronic Care Model (CCM) at the VNHS clinic improve HCV Care Cascade?

Methods: *The Intervention:* This Quality Improvement study is about adopting the CCM approach to HCV care, while employing an Indigenous world view throughout all phases of the research process. The HCV Care Cascade will be analyzed during and post implementing of the CCM based interventions.

Results: The ongoing interventions are as follows:

a) improving HCV related measures and data tracking,
b) engaging clients in peer support and wellness groups,
c) improving screening, monitoring and treating those affected by substance use disorder,
d) increasing HCV-nurse availability,
e) tracking and encouraging completion of fibroscan,
f) enhancing focus on women affected by HCV,
g) connecting those affected with Indigenous Elders for cultural healing/counseling if appropriate.

Discussion: To improve HCV Care in this context, a stepwise, quality improvement approach is required, implementing multi-prong, and coordinated group of interventions, which can be evaluated as impacting the HCV Care Cascade.

CSP3.15

Characteristics of Pneumonia Admissions in HIV Positive Individuals: A Single Centre 10 Year Cross-sectional Retrospective Analysis

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Background: A recent study from our centre identified pneumonia as the most common reason for admission in HIV positive individuals. The objective of the present study is to further characterize these admissions, including causative organisms, method of diagnosis and choice of initial empiric therapy.

Methods: Our centre's Medical Database was used to identify all HIV positive patients admitted to medical wards with a diagnosis of pneumonia from January 2005 to January 2015 in one tertiary care hospital, yielding a total of 389 admissions. Patient demographics were obtained through the Medical Database and supplemented with hospital chart reviews. At the time of abstract submission, a total of 79 admissions had been reviewed.

Results: The median CD4 count for 62/79 (78%) admissions was 119 (Q1 to Q3 = 38 to 283). For all admissions, an organism was isolated in only 37% (25/68). Regarding method of diagnosis during admission, only eight bronchoalveolar lavages (BAL) were performed. For admissions with an organism isolated, the most common organism was *Pneumocystis jirovecii* with a frequency of 16.2% of all admissions. We determined the initial choice of antibiotic therapy for each admission and further categorized it as following IDSA guidelines or not. For the 69 admissions where this data was available, 56% of physicians followed the IDSA guidelines.

Conclusions: For all hospital admissions, there was a low percentage of an isolated organism at only thirty-seven percent. Despite advanced HIV disease as determined by low CD4 count, less than 12% of admissions had a BAL performed. Only 56% of physicians followed IDSA guidelines for empiric antibiotic therapy for inpatient pneumonia. The IDSA guidelines do not address HIV positive individuals, suggesting a more important role for diagnostic methods in this population. The infrequent use of diagnostic BAL may contribute to low rate of etiological diagnosis and suboptimal antimicrobial therapy.

CSP3.16

The final frontier: Successful Treatment for HCV genotype 1 in those with HIV with access to treatment

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Background: Direct acting antivirals (DAAs) for hepatitis C (HCV) allow virologic cure for most. Experience in coinfec-

tion and advanced cirrhosis is more limited. We present data from a single centre to examine HCV treatment experience.

Methods: EMR database was queried for patients with HIV referred for HCV. Laboratory safety of DAA treatment was monitored at weeks 0, 2, 4, 8 and 12 of treatment. Individual records were reviewed to January 9, 2016.

Results: 112 coinfected patients have attended this clinic since 2012. Whereas only 9 individuals were treated with interferon and an HCV protease inhibitor (boceprevir, telaprevir or simepravir) in 2012 and 2013, 55 were treated with interferon-free regimens in 2014 and 2015 (table). 29/55 have achieved SVR12, 15 have completed therapy, and 9 have at least 4 weeks on-treatment follow-up. On treatment HCV viral load testing at weeks 2 and 4 did not predict outcome. No patient has failed therapy. SVR12 data are not yet available for one patient who discontinued early due to SAE (jaundice/liver failure) and one who with poor medication adherence (84 doses over 112 days) while actively injecting drugs. We identify a safety signal of elevated direct bilirubin without concomitant abnormality in liver enzymes that developed by week 2 of treatment in 3 of 5 on Lopinavir/ritonavir containing ARV.

Conclusion: HCV treatment with DAAs is effective and safe in HIV coinfection. Lopinavir/r should be avoided if possible while undergoing treatment with Sofosbuvir/Ledipasvir. The most significant challenge currently is access to medications because of high cost.

	SVR12 (N=29)	On treatment (N=26)
Sofosbuvir/Ledipasvir	28 (96.6%)	25 (96.1%)
Sex (M/F)	25/4	24/2
Age Mean years (range)	52.7 (32-71)	50.4 (27-66)
Ethnicity (White/Black/Other)	25/2/2	20/3/3
HCV genotype 1a	22 (75.9%)	22 (84.6%)
HCV viral load (baseline)	1.52E6 IU/mL	1.52E6 IU/mL
F3-4	16 (55.2%)	16 (61.5%)
CD4	563 (147-1470)	625 (164-1757)
cARTwith		
Tenofovir	23 (79.3%)	16 (61.5%)
Abacavir	7 (24.1%)	7 (26.9%)
NNRTI	10 (34.5%)	7 (26.9%)
PI/r	5 (17.2%)	10 (38.5%)
Integrase inhibitor	18 (62.1%)	11 (42.3%)
HCV PCR pos at week 2	6/28 (21.4%)	10/23 (43.5%)
HCV PCR pos at week 4	2/27 (7.4%)	5/20 (25%)

Complications of Antiretroviral Therapy
Complications des thérapies antirétrovirales

CSP4.01

Potential Synergistic Effect of Tesamorelin, a GHRH Analogue, and Fibrates to Decrease Triglycerides in HIV-Infected Patients with Excess Abdominal Fat

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Background: Growth hormone (GH) may decrease triglycerides (TG) through inhibition of de novo lipogenesis and increase in fatty acid oxidation. Tesamorelin, a stabilized analogue of growth hormone-releasing hormone (GHRH), has been shown to decrease visceral adipose tissue (VAT) and TG in HIV-infected patients with excess abdominal fat.

Objectives The objective of this post-hoc analysis was to determine whether the combination of tesamorelin with lipid lowering agents, including fibrates and statins, results in a synergistic effect that further reduces TG.

Methods: Data were analyzed from two randomized, placebo-controlled Phase 3 studies involving 806 HIV-infected patients with excess abdominal fat by analysis of covariance (ANCOVA).

Results: Baseline TG levels were 245.33±227.36 (mean±SD) and 228.30±144.28 mg/dL in the tesamorelin and placebo groups, respectively (P=0.26). The % of patients using LLT was similar between the two groups (45%). The % of patients using fibrates (7%) and statins (29%) was also similar between the 2 groups. Overall, TG decreased significantly in tesamorelin-treated patients vs. placebo (Δ Least Square Mean (LSM), -14.99%; 95% CI, -23.61 to -5.40). In patients not using LLT, the treatment difference for the % change from baseline to Week 26 in TG was -9.23% (95% CI, -16.16 to -1.74). The magnitude of the treatment difference was greater in patients on fibrates [Δ LSM, -25.43%; 95% CI, -40.70 to -6.24) as compared to patients on statins (Δ LSM, -12.5%; 95% CI, -21.53 to -2.42) or both fibrates and statins (Δ LSM, -14.45%; 95% CI, -31.69 to 7.15).

Conclusion: Taken together, these results suggest that tesamorelin may act synergistically with fibrates to decrease TG levels in HIV-infected patients with excess abdominal fat. Based on the pharmacological action of tesamorelin, it might be hypothesized that the increase in GH level induced by tesamorelin may result in increased fatty acid oxidation and thereby decreased TG level.

CSP4.02

Incidence of renal stones in persons treated with atazanavir versus other antiretrovirals: A population-based study

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Background: Single-clinic cohorts have identified increased risk of renal stones associated with the protease inhibitor (PI) atazanavir. This study's objective was to estimate the rate and relative risk of renal stones in persons receiving atazanavir versus other antiretroviral therapy (ART) in a longitudinal, population-based cohort.

Methods: HIV-1-infected, ART-naive persons age ≥19 years in British Columbia's "Comparative Outcomes And Service Utilization Trends" cohort were included if they initiated ART 01-Apr-1999 to 31-Mar-2011 and had ≥3 years pre-ART observation to identify baseline comorbidities and pre-ART stones.

ART categories were "atazanavir", "other-PI" (excluding indinavir) and "non-PI". Comorbidities and renal stones were identified by ICD-9/10 codes in hospitalization and ambulatory records. The hazard ratio (HR) for developing renal stones between ART categories was estimated by Cox proportional hazards regression, adjusted for covariates. Follow-up was censored at ART category change, death, loss-to-follow-up or 31-Mar-2013.

Results: The 3822 subjects were median (Q1-Q3) age 42 (35-48) years, 79% male and followed median 2.06 (0.62-4.23) years. There were 1002 atazanavir (99% ritonavir-boosted), 933 other-PI (lopinavir/ritonavir 70%, nelfinavir 20%) and 1887 non-PI (efavirenz 58%, nevirapine 36%). Persons with atazanavir-ART, older age and pre-ART stones had relatively higher renal stone rates (Table). Baseline comorbidities were strongly associated with pre-ART stones. When adjusted for age, sex and pre-ART stones, HR for renal stones was 1.75 (1.00-3.05) for atazanavir versus non-PI-ART, with no difference in stone rates for other-PI versus non-PI ART.

Conclusions: Consistent with other studies, atazanavir was associated with a modest increase in renal stone rate relative to other ART.

Table 1: Renal stone rates and bivariate analyses of renal stone HR by risk factor

Risk factor	Total N=3822 n (% of N) with Risk factor	# (% of n) with renal stone*	Renal stone rate/1000 p-yr (CI95%)	Unadjusted HR (CI95%)	Adjusted HR (CI95%)**
ART Category					
Non-PI	1887 (49.4)	27 (1.4)	4.54 (3.11-6.62)	1.00	1.00
Other-PI (not indinavir)	933 (24.4)	9 (1.0)	4.69 (2.44-9.02)	1.02 (0.48-2.17)	1.01 (0.47-2.17)
Atazanavir	1002 (26.2)	27 (2.7)	8.61 (5.90-12.55)	1.89 (1.11-3.23)	1.75 (1.00-3.05)
Age, (per year)				1.05 (1.03-1.07)	NA
Sex					
Female	800 (20.9)	10 (1.3)	6.38 (3.43-11.85)	1.00	NA
Male	3022 (79.1)	53 (1.8)	5.62 (4.29-7.35)	0.88 (0.44-1.73)	NA
Pre-ART renal stone*					
No	3713 (97.1)	51 (1.4)	4.74 (3.60-6.24)	1.00	NA
Yes	109 (2.9)	12 (11.0)	49.3 (28.00-86.81)	10.56 (5.61-19.89)	NA
Diabetes mellitus					
No	3603 (94.3)	54 (1.5)	5.31 (4.06-6.93)	1.00	NA
Yes	219 (5.7)	9 (4.1)	10.92 (5.68-20.99)	2.06 (1.01-4.18)	NA
Gout					
No	3726 (97.5)	61 (1.6)	5.73 (4.46-7.37)	1.00	NA
Yes	96 (2.5)	2 (2.1)	5.48 (1.37-21.92)	0.97 (0.24-3.96)	NA
Hyperpatrathyroidism					
No	3810 (99.7)	62 (1.6)	5.66 (4.41-7.25)	1.00	NA
Yes	12 (0.3)	1 (8.3)	25.35 (3.57-179.95)	4.11 (0.57-29.89)	NA
Inflammatory bowel disease					
No	3787 (99.1)	36 (1.7)	5.79 (4.52-7.41)	NA	NA
Yes	35 (0.9)	0 (0)	No events	NA	NA

ART: antiretroviral therapy; CI95%: 95% confidence interval; **HR:** Hazard ratio (Cox proportional hazards model); ****Adjusted HR**: Hazard ratio adjusted for age, sex, prior renal stone (multivariable Cox Proportional hazards model); **NA**: not applicable; **PI:** protease inhibitor, **p-yr:** person-years, **Q1-Q3:** 25th-75th percentile, ***Renal stone** identified by ICD-9 592, 594, 274.11, ICD-10 N20.x, N21.x, N22.x

CSP4.03

Longer Term Safety of Tenofovir Alafenamide in Renal Impairment

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Background: Tenofovir alafenamide (TAF) is a novel prodrug of tenofovir (TFV) that results in 91% lower plasma TFV levels compared to TDF. Switch to a once-daily single tablet regimen of elvitegravir, cobicistat, emtricitabine, and TAF (E/C/F/TAF) in HIV-1 infected patients with $eGFR_{CG}$ (Cockcroft-Gault) 30 to 69 mL/min was shown to be effective and safe through 48 weeks. Here, we report longer term results.

Methods: Virologically suppressed adults with stable $eGFR_{CG}$ of 30 to 69 mL/min had their treatment switched to open-label E/C/F/TAF. The primary endpoint was the change from baseline in eGFR at 24 weeks. Longer term efficacy and safety data are described, including tests of renal function and bone mineral density (BMD).

Results: Of 242 subjects enrolled, mean age was 58 years (range: 24 – 82), 39% hypertension, 14% diabetes, and 65% were taking TDF-containing regimens prior to switch. Through Week 72, minimal change in $eGFR_{CG}$ was observed. Five patients (2.0%) with baseline eGFR <50 mL/min discontinued study drug for decreased creatinine clearance, none had evidence of proximal renal tubulopathy and all had risk factors for renal disease progression (diabetes and poorly controlled hypertension). Subjects who received TDF at baseline had significant improvements in proteinuria and albuminuria to levels seen with non-TDF regimens. The prevalence of significant proteinuria (UPCR > 200 mg/g) and albuminuria (UACR ≥ 30 mg/g) decreased from 42% to 18% and 49% to 28%, respectively. Hip and spine BMD increased significantly (mean % changes from baseline +1.50 and +1.91, respectively, p<0.001). 93% maintained HIV-1 RNA <50 copies/mL based on Missing = Failure analysis.

Conclusions: Through 72 weeks, switch to E/C/F/TAF was associated with minimal change in $eGFR_{CG}$. Proteinuria, albuminuria and bone mineral density significantly improved. These data support the efficacy and safety of once-daily E/C/F/TAF in HIV+ patients with eGFR 30-69 mL/min without dose adjustment.

HIV and Aging and Comorbidities
Le VIH, le vieillissement et les comorbidités

CSP5.01

Outcomes among persons with HIV following acute myocardial infarction: a population-based study

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Background: There are limited population-based studies in Canada comparing mortality and access to care following acute myocardial infarction (AMI) among people with and without HIV. Accordingly, we compared mortality risk and health service use among people living with and without HIV in Ontario following an incident AMI between January 1, 2002 and March 31, 2013.

Methods: We conducted a population-based study using Ontario's health administrative databases. We used penalized likelihood logistic regression to compare the risk of death during hospitalization for AMI. In secondary analyses, we used Cox proportional hazard models to compare the cumulative incidence of: 1) receipt of revascularization procedures within 90 days of AMI; 2) readmission or emergency department visits for heart disease within 90 days of discharge; and 3) cardiologist follow-up within 90 days of discharge.

Results: We studied 220,365 AMI patients, of whom 279 (0.13%) were people with HIV. People with HIV were younger than HIV-negative individuals [mean age $\pm$ standard deviation: 54.1 $\pm$ 10.8 vs. 69.3 $\pm$ 14.3 years; standardized difference = 1.06]. Following multivariable adjustment, there was no difference in the risk of death during hospital admission [odds ratio 1.05; 95% confidence interval (CI) 0.64 to 1.64), receipt of revascularization procedure [hazard ratio (HR) 0.99; 95% CI 0.85 to 1.16), readmission or emergency department visit for heart disease (HR 1.09; 95% CI 0.76 to 1.56) or outpatient cardiology visit 90 days following discharge (HR 1.29; 95% CI 0.88 to 1.91). Stratification by age did not change the results appreciably.

Conclusion: Outcomes are similar among people with and without HIV following AMI. However, people with HIV experience AMIs at significantly younger ages than HIV-negative individuals, underscoring the importance of early interventions targeting modifiable risk factors for heart disease in these patients.

CSP5.02

Presence of complex comorbidity and functional disability when ageing with HIV; review of referrals to specialist HIV outpatient physiotherapy in the UK

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Background: A specialist HIV outpatient physiotherapy service provides individual treatment (1:1) and group treatment (Kobler rehabilitation class). Evaluation of referrals included access, patient profile, health and functional status, and treatments.

Methods: Over 24 months commencing October 2013, retrospective evaluation was completed from electronic documentation. Health and functional status were evaluated using ICD-10 online application and ICF checklist version 2.1a.

Results: We reviewed 137 patients; male (83%), median age 52 (range 29-77), HIV diagnosed >10 years (80%) and undetectable viral load (97%). Socially 61% unemployed, 71% lived alone, 64% lived locally to hospital and 87% did not meet UK physical activity recommendation. Referrals were mostly from HIV physician (47%), dietician (21%) or physiotherapist (8%) for musculoskeletal (53%), sedentary (12%) or neurological (9%) reasons. Patients lived with median 5 comorbidities (SD 2.4) and 87% meet definition of complex comorbidity; ≥2 additional chronic conditions in ≥2 different body systems. ICD-10 subgroups include "*diseases of musculoskeletal system and connective tissue*" (21%), "*mental and behavioural disorders*" (13%), "*endocrine, nutritional and metabolic diseases*" (11%) and "*diseases of the nervous system*" (11%). ICF body function impairments were "*pain*" (88%), "*mobility of joint*" (75%) and "*emotional function*" (71%). ICF body structure impairments were "*movement of lower extremity*" (64%), "*movement of trunk*" (53%) and "*spinal cord and peripheral nerves*" (32%). ICF activity limitation and participation restriction were "*recreation and leisure*" (72%), "*walking*" (56%) and "*remunerative employment*" (50%). ICF environmental factors were "*social security*" (27%), "*products for indoor/outdoor mobility*" (22%) and "*immediate family*" (18%). Treatments were provided mostly in combination (55%) with 56% requiring 1:1 treatment and 53% accessing the Kobler rehabilitation class. Patients attended mean 1.8 (range 1-6) 1:1 sessions.

Conclusion: Patients referred to specialist HIV Physiotherapy present with complex comorbidity, when ageing with well-controlled HIV. The presence of multiple comorbidities was observed with high prevelence of functional disability.

CSP5.03

People living with HIV have worse health status than elderly people at risk of hospitalisation, when referred to specialist HIV outpatient physiotherapy in the UK

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Background: EQ-5D-5L health status measures 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. A specialist HIV outpatient physiotherapy service, located in a specialist HIV centre, provides individual treatment (1:1) and group treatment (Kobler rehabilitation class).

Methods: Over 24 months commencing October 2013, EQ-5D-5L was completed in all referred patients. Change in EQ-5D-5L was evaluated with paired t-test at the end of 1:1 physiotherapy.

Results: We reviewed 137 patients; male (83%), median age 52 (range 29-77), HIV diagnosed >10 years (80%) and undetectable viral load (97%). Pre-intervention EQ-5D-5L values (table 1) and index (0.44), demonstrate worse health status compared to UK population, HIV outpatients and elderly people at 12 month hospitalisation risk. 76 (56%) patients received 1:1 physiotherapy alone (n=15, 11%) or in combination (n=61, 45%) with other interventions. Data was excluded if patients DNAd (n=29, 21%) or treatment continued (n=11, 8%). EQ-5D-5L was repeated in 22 (16%) at cessation of 1:1 physiotherapy alone (n=15, compliance 100%) or combination interventions (n=7, compliance 11%). Post-intervention EQ-5D-5L observed significant improvement in mobility (p=0.002), usual activities (p=0.01), pain/discomfort (p=0.001) and anxiety/depression (p=0.03) with improved median scores (table 1) and index (0.68).

Conclusion: There is high prevalence of poor health status in adults with HIV attending specialist HIV physiotherapy. Significantly improved health status was observed in mobility, usual activities, pain/discomfort and anxiety/depression, in patients completing 1:1 physiotherapy alone or in combination with group treatment. Specialist HIV physiotherapy, located in specialist HIV centres, can support multi-dimensional care to optimise health and well-being.

Table 1: EQ-5D-5L distribution, n(%)

	Mobility	Self-Care	Usual Activities	Pain/ Discomfort	Anxiety/ Depression
Pre- Intervention					
No problem	27 (20)	60 (44)	26 (19)	14 (10)	25 (18)
Mild	34 (25)	40 (29)	33 (24)	26 (19)	32 (23)
Moderate	49 (36)	29 (21)	54 (39)	46 (34)	41 (31)
Severe	25 (18)	8 (6)	19 (14)	40 (29)	29 (21)

Extreme or unable	2 (1)	0 (0)	5 (4)	11 (8)	10 (7)
% any problem	80	56	81	90	82
Median level	3.0	2.0	3.0	3.0	3.0
Post- Intervention					
No problem	10 (45)	14 (64)	10 (46)	6 (27)	11 (50)
Mild	7 (32)	4 (18)	6 (27)	7 (32)	6 (27)
Moderate	3 (14)	3 (14)	5 (23)	6 (27)	4 (18)
Severe	2 (9)	1 (5)	1 (5)	3 (14)	0 (0)
Extreme or unable	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)
% any problem	55	37	55	73	50
Median Level	2.0	1.0	2.0	2.0	1.5

CSP5.04

Improved function, strength, quality of life & goal attainment in people with HIV attending UK specialist physiotherapy-led group rehabilitation intervention

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Background: A specialist HIV outpatient physiotherapy service, provides individual treatment (1:1) and group treatment (Kobler rehabilitation class). The Kobler rehabilitation class combines physiotherapy-led group exercise and education, twice week for 10-weeks. We evaluated referral patterns, rehabilitation goals, adherence and measurement change.

Methods: Over 24-months commencing September 2012, 92 patients were measured for functional capacity (6-minute walk test; 6MWT), flexibility (sit and reach test), upper and lower limb strength (1-repetition max) and health related quality of life (HRQOL) using Functional Assessment of HIV infection (FAHI). Adherence was defined as attending ≥8/20 sessions. Rehabilitation goals were themed and progression quantified using Goal Attainment Scale (GAS). Reasons for non-adherence were identified by retrospective telephone interview.

Results: At baseline, referrals were for musculoskeletal (25%), oncological (20%) or cardio-metabolic (19%) reasons among a male (82%), Caucasian (71%) and ageing (mean 51.5 years) cohort. Themed rehabilitation goals included improving body image, participation, mobility, health/fitness and function. Adherence was achieved by 46%, with open access utilised by 37%; returning (n=19) or restarting when non-adherent (n=15). Reasons for non-adherence, identified in 21 (42%) of 50 non-adherent, related to physical/mental health, individual factors like exercising independently, or class features such as time/location. Post-intervention measurement in 37 (40%) demonstrated improvements in 6MWT distance ($p<0.001$), flexibility ($p<0.001$), strength in triceps ($p<0.001$), biceps ($p<0.001$), lattisimus dorsi ($p<0.001$), shoulder-press ($p<0.001$), chest-press ($p<0.001$), and leg-press ($p<0.001$). HRQOL improved in total score ($p<0.001$), physical ($p<0.001$), emotional ($p<0.001$) and functional ($p=0.065$) subscales. GAS quantified 83% goals scoring "expected" (n=57), "somewhat more" (n=31) or "much more" (n=14) level of achievement.

Conclusion: This Kobler rehabilitation class improved functional capacity, strength, flexibility, HRQOL and goal attainment, among those completing the intervention. Sub-optimal adherence likely relates to episodic disability, highlighting the importance of rehabilitation interventions to be flexible, allowing individuals to attend dependent on their episodes of health and disability.

CSP5.05

Rapid Decrease in Leukocyte Telomere Length Following HIV Seroconversion, but not HCV Seroconversion

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Background: Age-related diseases are more prevalent in persons living with HIV, suggesting accelerated aging. Both HIV and hepatitis C virus (HCV) infection have been associated with shorter leukocyte telomere length (TL). Whether this apparent telomere shortening occurs immediately following HIV and/or HCV seroconversion or over time throughout the chronic infection period is unclear.

Methods: Subjects were from the Vancouver Injection Drug Users Study (VIDUS). TL was measured in PBMC pellets from 95 VIDUS participants who subsequently acquired HIV (n=51) or HCV (n=16) at 2 time points: a median of 3 months before seroconversion and a median of 9 months after seroconversion. Control participants who did not seroconvert (NS) for either virus (n=29) were analyzed at 2 random time points a median one year apart. TL was assayed randomly and blindly via monochrome multiplex qPCR, yielding a relative ratio (Telomere/Reference DNA) proportional to average TL. Within-individual TL change between the two time points were compared for each group using the Wilcoxon signed rank test.

Results: TL was significantly shorter (-13%) post-seroconversion compared to pre-seroconversion in those who acquired HIV [Median 8.2 (6.9-10.0) vs 9.1 (7.7-11.1), $p=0.025$], but not in HCV seroconverters [8.4 (7.2-9.9) vs 8.5 (6.9-10.0), $p=0.552$] or control non-seroconverters [9.6 (8.8-11.2) vs 9.6 (8.7-11), $p=0.353$]. Among HCV seroconverters, 31% (5/16) were already HIV+ while 90% (46/51) of the HIV seroconverters were already HCV+. One subject serocon-

verted for both viruses. Median age for HIV, HCV and NS subjects were 36, 29 and 24 years, respectively.

Conclusions: Apparent PBMC TL shortening occurs shortly after HIV seroconversion. This could result from a preferential loss of cells with long TL, TL shortening in precursor cells, or widespread telomere damage. The association between HCV and shorter TL may be primarily driven by chronic infection. All could influence aging and immunosenescence.

CSP5.06

Evidence of monocyte inflammation in HIV+ patients on effective combination antiretroviral therapy

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Introduction: With combination antiretroviral therapy (ART), the life expectancy of people living with HIV infection is near normal and it is now estimated that nearly half of all HIV+ individuals on ART are >50 years of age. With this, co-morbidities associated with aging are becoming evident in this patient population and chief among them is cardiovascular disease. There is compelling evidence that atherosclerosis is an inflammatory condition involving the vascular endothelium resulting in monocyte activation and infiltration of the vessel wall. In view of this, our objective here was to characterize the inflammatory state of monocytes in HIV+ patients on effective ART.

Methods: Markers of inflammation (CD127 and CD16) were measured by flow cytometry on CD14+ monocytes isolated from HIV+ patients on ART with suppressed viral loads.

Results: HIV+ patients on effective ART have a significantly greater proportion of circulating pro-inflammatory CD16+ monocytes (37%+/-5%) compared to healthy controls (15%+/-2%), a finding previously linked to cardiovascular disease in the general population. We also found monocytes isolated from HIV+ individuals on ART have higher CD127 expression (32%+/-3%) compared to those from healthy controls (11%+/-5%), a finding linked to a number of inflammatory diseases such as Rheumatoid Arthritis.

Conclusion: Several studies have now demonstrated HIV+ individuals have a 2-4 fold increased risk of cardiovascular disease, likely due to chronic inflammation. Consistent with this, we have found HIV+ patients on effective ART have a higher proportion of circulating pro-inflammatory monocytes, cells known to contribute directly to atherosclerotic plaque formation. Our data will next be correlated with aortic inflammation by FDG-PET/CT and with coronary flow reserve as measured by myocardial contrast echocardiography. We will also examine the effect of rosuvastatin in monocyte and cardiovascular inflammation. These data then may provide an early indication for statins as primary prevention of CVD in HIV+ patients.

CSP5.07

Impact of Expanded Access to Highly Active Antiretroviral Therapy on Chronic Comorbidities among HIV-Positive individuals in British Columbia

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Background: Expanded access to early highly active antiretroviral therapy (HAART) has proven beneficial in reducing both non-HIV and HIV related morbidity and mortality. We designed a study to characterize how HAART expansion in British Columbia (BC) has affected the risk of chronic comorbidities.

Methods: Our analysis was performed using an administrative population-based dataset of HIV-positive individuals (≥19 years) in BC. Using ICD-9/10 codes derived from physician billing claims and hospitalization discharges for case identification, we determined the RR of disease incidence among HIV-positive, BC-residents, receiving HAART during the study period (2000 to 2012). We determined the ratio of disease incidence for the following six diseases in individuals whom initiated HAART in the post- (2006-2012) compared to the pre- (2000-2005) HAART expansion periods: cardiovascular disease (CVD), diabetes mellitus (DM), hypertension (HTN), asthma/chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD) and chronic liver disease (CLD). Poisson's regression analysis was used to measure RRs.

Results: The study cohort (n=4,840) was predominantly male (80%) with a median CD4 cell count of 220 cells/μL and log-10 plasma viral load of 4.89 copies/ml at HAART initiation. Between 2000-2012, CLD incidence decreased (RR of 0.67; 95%CI: 0.55, 0.82) when comparing post- relative to pre-HAART expansion periods. For CVD, DM, HTN, COPD/asthma and CKD we did not detect any significant differences in disease incidence (Table 1).

Conclusions: We observed decreases in population-level CLD incidence among HIV-infected individuals in the post-HAART expansion period in BC but no significant differences in incidence for other chronic diseases.

Table 1: Relative Risks for chronic disease incidence of individuals after HAART expansion relative to individuals before HAART expansion with associated 95% CI (adjusted by covariates: age, sex, first regimen drug class, baseline weighted CCI, log-10 pVL and CD4 cell count)

	Crude RR	Adjusted RR
Outcome		
CVD	0.74 (0.54, 1.03)	0.77 (0.55, 1.08)
COPD	0.96 (0.71, 1.30)	0.92 (0.68, 1.26)
DM	1.34 (0.90, 2.00)	1.33 (0.89, 2.00)

HTN	1.35 (0.98, 1.87)	1.36 (0.98, 1.90)
CKD	0.68 (0.36, 1.27)	0.65 (0.34, 1.24)
CLD	0.63 (0.52, 0.77)	0.67 (0.55, 0.82)

RR: relative risk; HAART: highly active antiretroviral therapy; CVD: cardiovascular disease; DM: diabetes mellitus; HTN: hypertension; COPD: chronic obstructive pulmonary disease; CKD: chronic kidney disease; CLD: chronic liver disease; pVL: plasma viral load; CCI: Charlson Comorbidity Index; CI: confidence interval

CSP5.08

Factors Associated with Incidence of Diabetes Mellitus (DM) in Older HIV Positive Patients

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Objectives: To determine the incidence of and factors associated with DM in an aging HIV+ cohort.

Methods: Data were collected since February 1987 from patients attending a large HIV clinic in Vancouver, BC. The analysis included those who were aged ≥50 years as of July 31, 2015. DM was defined as having ≥1 of: random blood sugar ≥ 11.1 mmol/L, fasting blood sugar ≥ 7 mmol/L, HbA1C ≥ 6.5%, or use of anti-diabetic medications during the follow-up period. Logistic regression was used to estimate the probability of developing DM, adjusting for demographic and clinical factors.

Results: The analysis included 1118 patients: 90% male, 79% Caucasian, 11% Aboriginal, 26% with history of injection drug use, and 38% hepatitis C co-infected. Median age at antiretroviral (ART) initiation was 44 (IQR 38, 50) years, and at DM diagnosis was 54 (IQR 50, 60) years. After median follow-up of 13 (IQR 9, 18) years, 294 developed DM (incidence rate 2.1 per 100 person-years). Age ≥50 years at ART initiation, earlier year of ART initiation, and lower CD4 nadir were associated with having DM at the end of follow-up (Table). Neither time on any ART class nor hepatitis C co-infection was associated with DM.

Conclusions: The incidence of DM among HIV+ patients aged ≥50 years was 2.1 per 100 person-years, 1.8 times higher than the age-matched Canadian population (1.16 per 100 person-years). Older age at ART initiation, longer duration of ART, and lower CD4 nadir were associated with a higher likelihood of developing DM.

Table. Factors associated with development of DM in an HIV+ cohort (N=1118)

	Adjusted Odd Ratio	95% Confidence Interval
Age of ART initiation		
< 50 years	Reference	
> 50 years	1.45	1.00, 2.10
Year of ART initiation		
Before 1996	Reference	
1996 to 1999	1.04	0.74, 1.46
2000 to 2004	0.79	0.52, 1.20
2005 to 2009	0.29	0.17, 0.49
2010 to 2015	0.06	0.02, 0.20
CD4 nadir (per 100 cells/mm^3)	0.85	0.72, 1.00

CSP5.09

Associations Between White Matter Hyperintensities (WMH) and Neuropsychological Performance for Individuals with HIV

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Background: About 52% of individuals with HIV have neuropsychological impairments, particularly processing speed and executive dysfunction. These symptoms have been associated with WMH in various patient populations.

Objective: To examine associations between WMH and cognitive tasks for individuals with HIV.

Methods: Individuals were recruited from the HIV Neurocognitive Disorder Clinic in Vancouver and provided consent to participate in this study. They had neuropsychological testing and a brain MRI from which modified Fazekas ratings of WMH were made (0-3 ratings for each of 8 locations). Pearson correlations were performed between Fazekas total deep white matter rating (DWM), total periventricular white matter rating (PVWM), and total overall rating (TOTWM) scores and selective neuropsychological tests: Digit Span (auditory attention, n=47), Auditory Consonant Trigrams (ACT, multitasking, n=35), Trail Making Test-Part A (TMT-A, processing speed, n=47) and B (TMT-B, speeded alternate sequencing, n=45), and Stroop Colour-Word test (Stroop, speeded response inhibition, n=28).

Results: The 47 participants had a median age of 53 (interquartile range [IQR]=48-58) and education of 14 years (IQR=12-16). Table 1 shows significant correlations with WMH rating and ACT and Stroop as well as a trend for TMT-A. TOTWM and DWM had significantly skewed distribu-

tions so square root transformations were performed; ACT and Trails A were significantly correlated with transformed WMH scores.

Conclusions: Results indicated associations between processing speed and multitasking performance with DWM as well as speeded response inhibition with PVWM. As such, there may be differential associations for certain cognitive abilities and location of white matter changes.

Table 1. Notable Correlations

Variables	r	p
ACT and TOTWM	-0.395	<0.01
ACT and DWM	-0.477	<0.005
Stroop and PVWM	-0.397	<0.05
TMT-A and TOTWM	-0.208	0.081
TMT-A and DWM	-0.192	0.098
ACT and transformed TOTWM	-0.360	<0.05
ACT and transformed DWM	-0.457	<0.005
TMT-A and transformed TOTWM	-0.252	<0.05
TMT-A and transformed DWM	-0.284	<0.05

CSP5.10

Associations between HIV-related factors and neurocognitive impairment based on results of two validated screening tests among HIV+ adults treated with HAART

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Background: Although HIV-associated dementia is less common in the HAART era, subtle neurocognitive impairment may be present in HAART-treated individuals. Brief cognitive tests may play a role in screening.

Objective: To evaluate cognitive performance on the Montreal Cognitive Assessment (MoCA) and HIV Dementia Scale (HDS) and their association with HIV/HAART-related factors.

Methods: HIV+ adults with any degree of self-reported impairment in cognition, memory and concentration not explained by another diagnosis were referred for comprehensive evaluation and recruited for this cross-sectional, cohort study. MoCA and HDS were administered on the same day; abnormal scores are ≤ 25 and ≤ 9, respectively. HIV/HAART-related factors were derived from the provincial Drug Treatment Program which provides HAART to HIV+ adults. Fisher's exact test was used for categorical values and Wilcoxon rank sum test for continuous variables.

Results: 81 adults were included in the main cohort and 74 had both MoCA and HDS scores (Table 1). A positive correlation was seen between MoCA and HDS scores ($r = 0.600$, $p < 0.001$). Abnormal HDS score was significantly correlated with current CD4+ count ($p = 0.040$). However, there was no significant correlation of either score with age, history of AIDS-defining illnesses, hepatitis B/C co-infection, nadir CD4+ count, baseline and current plasma viral load, duration of HIV diagnosis or time on HAART.

Conclusions: Both the MoCA and HDS were useful in identifying cognitive deficit in this symptomatic HAART-treated population. However, the observed cognitive dysfunction was not associated with HIV/HAART-related factors, suggesting other etiologies may be more important.

Table 1: Characteristics of study population (N=74)

Category	Value	Interquartile Range
Median age, years	52	46-59
Male gender, N (%)	69 (93%)	
Previous AIDS-defining illness, N (%)	35 (47.3%)	
Median current CD4+, cells/mm3	485	380-720
Median CD4+ nadir, cells/mm3	150	60-240
Median time since HIV diagnosis, years	10.2	6.0-16.4
Median duration on HAART, years	5.7	3.0-9.3
Ever diagnosed with Hepatitis B, N (%)	2 (2.7%) (8 unknown)	
Ever diagnosed with Hepatitis C, N (%)	22 (29.7%)	
Median MoCA score	23	21-27
Median HDS score	12	8-16
Abnormal MoCA score (≤ 25), N (%)	49 (66.2%)	
Abnormal HDS score (≤ 9), N (%)	25 (33.8%)	

CSP5.11

Will the next generation of rehabilitation professionals be ready to treat people living with HIV?: Results of a survey of UK Higher Education Institutions

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Objectives: Increasing co-morbidities in an aging HIV population increases the need for rehabilitation. Rehabili-

tation is commonly provided by physiotherapists and occupational therapists in both HIV specific and, increasingly, more generic settings. Future generations of therapists will require knowledge and skills to effectively treat people living with HIV. This study aims to examine the current provision of HIV education in pre-registration courses in the United Kingdom (UK).

Methods: We contacted 16 higher education institutions (HEIs), completing a telephone interview with the Course Leader, or equivalent, for any pre-registration physiotherapy or occupational therapy courses they provide. In total, 9 occupational therapy (OT) and 17 physiotherapy courses were reported on. The questions included a description of the nature of HIV related education provided and the amenability to expanding HIV content in future.

Results: Of the 26 courses reported on, 10 (38%) include formal HIV teaching content. Formal teaching lasted between 2 and 3 hours and in 6 instances were provided by HIV specialists, in 2 by internal lecturers and in 2 by students. Of the courses that offer no formal teaching content, most reported some opportunity to address HIV as part of project work or preparation for placement. All of the respondents reported that they had interest in an online module. Five respondents cited insufficient capacity within the curriculum for new subject matter. The survey process generated three invitations to provide face to face teaching.

Conclusion: Results from this preliminary study suggest considerable variance in the provision of HIV related education across the UK in OT and physiotherapy pre-registration courses, with a trend towards limited content in many courses. This is at odds with the projected increase in need and the tendency for many HEIs to provide condition-specific education for other conditions. Further work is required to establish a coordinated strategy.

CSP5.12

Greater Gastrointestinal Symptom Distress Negatively Impacts Health-Related Quality of Life: Results from the Ontario HIV Treatment Network Cohort Study (OCS)

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Background: Distressing gastrointestinal symptoms (GIS) are reported by two-thirds of Ontario HIV patients. However, no studies have examined effects of GIS on health-related quality of life (HRQOL) in HIV positive individuals.

Methods: The OCS is a multi-site HIV clinical cohort. Data collection includes chart review, interviews, and laboratory record linkage. Among participants interviewed in 2007-14 who completed the ACTG Symptom Distress Module and Medical Outcomes Survey SF-36, we calculated SF-36 mental (MCS) and physical (PCS) component summary scores (range 0-100; higher score indicates better HRQOL). Occurrence/distress for GIS (diarrhea/soft stool, nausea/vomiting, bloating, loss of appetite, and weight loss/wasting) were scored from 0 (not reported) to 4 (very bothersome). Effect size (beta) and 95% confidence intervals (CI) were estimated for GIS on MCS and PCS, adjusted for socio-demographic, behavioural, and clinical factors, using linear mixed models with a spatial power correlation structure.

Results: Among 1753 participants at baseline, 78.2% were male, aged 45 (IQR 35, 52) years, 57.8% MSM, 70.3% had viral load <50 copies/mL, and CD4 count of 457 (IQR 315-622). Participants had a median of 3 interviews (IQR 1-5). Minimally sufficient differences in composite scores were not observed from baseline (MCS: 49.0 [IQR 36.4, 55.7]; PCS: 49.0 [IQR 36.4, 55.7]) to last interview (MCS: 51.4 [IQR 44.6-55.0]; PCS: 50.7 [38.5-56.9]). GIS scores negatively correlated with HRQOL (Table).

Conclusions: These findings highlight the continued challenge of GIS occurrence and distress despite modern clinical management. Addressing GIS in HIV patients are of importance to optimize HRQOL among people living with HIV.

Table. Adjusted regression parameters of associations between gastrointestinal symptoms and SF-36 Health Related Quality of Life component scores among participants in the OHTN Cohort Study, 2007-2014.

	Mental Component Score (MCS)	Physical Component Score (PCS)
Symptom	Adjusted Beta (95% CI)	Adjusted Beta (95% CI)
Diarrhea/soft stool	-0.35 (-0.57, -0.13)	-0.52 (-0.68, -0.38)
Nausea/vomiting	-0.60 (-0.87, -0.33)	-0.64 (-0.81, -0.45)
Loss of appetite	-1.55 (-1.80, -1.30)	-0.48 (-0.65, -0.30)
Bloating	-1.04 (-1.25, -0.84)	-0.55 (-0.69, -0.41)
Weight loss/wasting	-1.06 (-1.31, -0.81)	-0.35 (-0.52, -0.18)

CSP5.13

A Meta-Analysis of the Incidence of Colorectal Cancer in Persons with HIV

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Background: In Ontario, colorectal cancers are the second most common cancers in men and third most common

cancers in women. Yet, the incidence of colorectal cancer among persons with HIV relative to the general population is poorly characterized. These data are necessary to inform guidelines for colorectal cancer screening for this population. Accordingly, we conducted a meta-analysis estimating the standardized incidence ratio of colorectal cancer among persons with HIV compared to the general population.

Methods: We conducted a systematic search across multiple electronic databases for English language articles from January 1, 1983 to April 20, 2015. All titles and abstracts were reviewed independently by two investigators with data extraction being performed by those meeting inclusion criteria. We included all studies reporting standardized incidence ratios (SIRs) of colorectal cancer in persons with HIV or data sufficient for estimating SIRs. We used random effects meta-analysis to estimate the pooled SIR and 95% confidence interval (CI). Studies were reviewed critically for quality.

Results: We identified twelve eligible studies (0.16%) from a total of 7,370. Overall, 460 cases of colorectal cancer occurred among 542,620 individuals with HIV. In meta-analysis, the incidence of colorectal cancer was similar among people with and without HIV (SIR 1.2; 95% confidence interval 0.7 to 2.0). Inclusion of 4 additional studies of incident colon cancer (excluding cancer of the rectum) did not change results appreciably (SIR 1.1; 95% CI 0.7 to 1.7).

Conclusion: Rates of colorectal cancer are similar among people living with and without HIV. Current guidelines for colorectal cancer screening may be sufficient for the HIV infected patient. However, further research characterizing and quantifying heterogeneity in stage at diagnosis, treatment outcomes, and colorectal cancer-related mortality among persons with HIV is needed.

CSP5.14

Cytokeratin 18 and Transient Elastography with Controlled Attenuation Parameter as Screening Tools for Nonalcoholic Steatohepatitis in HIV Mono-Infection

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Background: Nonalcoholic steatohepatitis (NASH) is a leading cause of end-stage liver disease in Canada. HIV+ persons are at risk of NASH. However, data on NASH in HIV mono-infection are scarce.

Methods: We conducted a prospective screening study for NASH in HIV mono-infected persons based on a stepwise diagnostic algorithm employing the serum biomarker cytokeratin 18 (CK-18) and transient elastography (TE) with associated controlled attenuation parameter (CAP). All patients underwent TE with CAP to diagnose fatty liver; patients with fatty liver were further screened for NASH with CK-18; finally, those with a non-invasive diagnosis of NASH were offered liver biopsy, as per standard of care. Fatty liver was defined as CAP>232dB/m. NASH was diagnosed by a CK-18>246U/L. Cofactors associated with NASH were determined by logistic regression.

Results: 310 cases (mean age 49.9 years, 77% men, mean CD4 630±253, 90% on antiretrovirals) without significant alcohol intake or coinfection with hepatitis B or C were included. Fatty liver was diagnosed by CAP in 171 cases (55%). CK-18 was performed in all of them, and NASH was diagnosed in 30 cases (representing 18% of patients with fatty liver and 10% of the overall cohort, a figure that is three times higher than the general Canadian population). 19 out of 30 patients with a non-invasive diagnosis of NASH agreed to undergo a liver biopsy. Histology confirmed NASH in all cases. After adjusting for age and BMI, ALT (OR=1.11, 95% CI 1.05-1.78; p<0.001) and TE measurement (OR=1.31, 95% CI 1.02-1.67; p=0.03) were independent predictors of NASH.

Conclusion: A screening strategy based on a stepwise algorithm combining two non-invasive tools and liver biopsy revealed a high prevalence of NASH in HIV mono-infected persons, particularly in case of high ALT and TE measurement. Non-invasive screening for NASH can help early diagnosis and initiation of interventions in this population.

HIV in Children and Adolescents
Le VIH chez les enfants et les adolescents

CSP6.01

Realizing Youth Potential: A New Group Clinic Model to Facilitate Improved Adherence and Outcomes among Youth with HIV

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Background: Youth with HIV have lower rates of engagement in care, medication adherence, and virologic suppression than other age cohorts. In British Columbia, <40% of youth with HIV (<30 years of age) are virologically suppressed. Youth are especially vulnerable to stigma and isolation, further impacting their engagement in care and health outcomes. An interdisciplinary women and family HIV clinic following both perinatally- and horizontally-infected youth was the setting for an innovative pilot project to enhance engagement in care.

Methods: A year-long pilot project of youth-specific group clinics began in July 2015. The population was divided into two cohorts (14-19 years and 20-29 years), each meeting quarterly. Each clinic consists of a brief medical visit fol-

lowed by a youth-led gathering facilitated by our partner organization, YouthCO, including an education session, meal, and social activity outside of clinic. Outreach workers offer transportation. Quantitative (number of youth engaged, virologic suppression) and qualitative (quarterly session-specific feedback, and end of pilot project interviews and focus groups) evaluation methods are being used.

Results: The two cohorts have each met twice to date. Attendance has increased with each subsequent group clinic. The younger cohort (perinatally-infected youth) has had 4-8 participants each session. Attendance for the older cohort was initially low but numbers are increasing. Initial qualitative feedback from youth has been consistently positive. Themes arising from feedback to date include feeling safe, welcome, and belonging to a group.

Conclusion: This model of youth group clinics demonstrates potential to connect, engage, and support youth. Participants report some early signs of benefit (such as feeling part of a group) which may reduce stigma and isolation and contribute to improved health outcomes. Longer follow up and data analysis at pilot project end is needed to determine the impact on emotional & mental health, quality of life, and virologic suppression rates.

CSP6.03

IFN-gamma Responses against HIV-1 Gag in Children with Long-Term Viral Suppression

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Background: Children with vertical HIV infection treated soon after birth with combination antiretroviral therapy who maintained long-term sustained viral suppression (SVS) have been reported to not develop HIV-specific cell-mediated immunity (CMI). We evaluated these responses in relation to HIV reservoir size in 5 early-treated children.

Methods: PBMC were obtained from 5 HIV-infected children with SVS (<50 copies/mL) who started cART within 24h of birth. At the time of sampling, SVS had been maintained for 3.7-8.4 years in Cases 1-4. Case 5 had rapid viral rebound after treatment interruption at 3 years with sustained suppression following treatment re-initiation (re-suppressed for 10 months at sampling). IFN-γ production in response to HIV-1 Gag clade-matched peptide pools was measured using ELISpot. HIV reservoir size was estimated using qRT-PCR for total and integrated HIV DNA and TILDA.

Results: HIV-specific IFN-γ responses were detected in all 5 children (0-121, 0-98, 0-165, 0-98, 0-492 spot-forming units (SFU) per pool per 10^6 PBMC in Cases 1-5) at levels markedly lower than in subjects without SVS (0-1858 SFU per pool per 10^6 PBMC) or responses to CMV and VZV. Two children's reservoir size was below limit of detection (LOD) by qRT-PCR and TILDA. One had 378 HIV copies/10^6 CD4 cells (integrated DNA and TILDA <LOD) and another had 1.4 infected cells/10^6 CD4 cells detected using TILDA (total and integrated DNA <LOD). Case 5 had 32 copies of integrated HIV DNA/10^6 CD4 cells and 119 copies of total HIV DNA/10^6 cells detected (TILDA <LOD).

Discussion: Low frequencies of IFN-γ-producing cells were detected in early-treated children with SVS upon stimulation with HIV-1 peptides. Case 5 (treatment interruption) exhibited intermediate responses relative to subjects with SVS and controls. HIV-1 reservoir was very small in all early-treated children. The role of CMI in long-term control of HIV in vertically-infected children requires further study.

CSP6.04

Impact of Low Level Viremia on Virological Failure in HIV-1 Infected Children Undergoing Antiretroviral Therapy

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Background: Successful HIV virological response to Antiretroviral Therapy (ART) is indicated as suppression of plasma Viral Load (VL) to undetectable level, while Virologic Failure (VF) occurs when ART fails to maintain suppression of VL at <1000 cp/mL. Notably, a portion of patients maintains persistent Low Level Viremia (LLV), VL between 50-1000 cp/mL, for over 6 months while on ART. LLV is indicative of incomplete viral suppression, which may create favorable situation for the development of Drug Resistance Mutations (DRMs). The challenges of HIV LLV are most profound in children in whom the dynamics of the interactions among the virus, the host and ART may be drastically different from those in adults. This projects aims to investigate the association between LLV and VF and to predict the risk factors causing VF in LLV children.

Methods & Results: A total of 2,900 HIV-1 infected children/adolescents enrolled in Leo Toto program – a multi-center community outreach program in Nairobi, Kenya, were included in this study. The demographic and clinical data including VL, ART regimen, and adherence were collected for these subjects from eight participating clinics. The patients were then categorized by their VL level and VF status. Chi-square analysis was used to test the association of LLV with VF and a significant association was found ($p < 0.01$) confirming that persistent LLV may increase the

risk of VF. Other key risk factors (ART regimen, DRMs, WHO stage, adherence, co-infections) will be evaluated with further statistical analysis.

Conclusion: This large cohort study provides convincing data on the association between LLV and VF in HIV patients at young ages. Our preliminary analysis suggests a relationship between LLV and VF. Further study will follow to examine the roles of HIV DRMs and other potential contributing factors, such as ART adherence, in this observed phenomenon.

CSP6.05

The Second-Generation of HIV-1 Vertically Exposed Infants: Challenges in their Management and Long-Term Care

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Background: Due to a lifetime of antiretroviral drug exposure, pregnancies among perinatally infected women represent a new challenge in the prevention of mother-child transmission of HIV. The objective of this study was to document health outcomes and challenges in the management of the second-generation of HIV-1-Exposed Uninfected (HEU) infants.

Methods: Clinical records from the Centre Maternel et Infantile Sur le SIDA (CMIS) mother-child cohort were reviewed to identify all pregnancies and live births among perinatally infected women previously followed as children at either CHU Sainte-Justine, or the Montreal Children's Hospital.

Results: Out of a total of 16 pregnancies among 12 perinatally infected women, there were 11 live births, 4 terminations, and 1 miscarriage. Median maternal age at first pregnancy was 20 (range 19-23 years). At the first prenatal visit, 91% had a detectable viral load (median 33 715 copies/ml, range 933-202250 copies/ml), and were not on antiretroviral therapy. At the time of delivery, 58% still had detectable viral load, and over half (55%) were immunosuppressed (CD4 count<200 cells/mm^{3}). All of the HEU newborns received 2 or more drugs for prophylaxis. Due to maternal drug resistance, this included regimens not approved for use in neonates. Mean gestational age was 39.1 weeks (range 35-40) and mean birthweight was 3241g ±521. Infants have been followed for a mean 43 months (range 4-100) and all are HIV negative. Of the 7 HEU infants now over age 2, 6 have been diagnosed with significant developmental delay (speech/language delay, n=4, autism confirmed n=1, autism suspected n=1).

Conclusions: Difficulties with adherence, drug resistance, and immunosuppression were identified challenges in the management of perinatally infected women during pregnancy. While longitudinal follow-up of their infants is underway, early results suggests high risk of developmental delay for this second-generation of HEU infants, warranting early developmental assessment and intervention.

CSP6.06

"Read to succeed": Literacy promotion for HIV exposed infants and children

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Background: Perinatally HIV exposed infants are vulnerable to developmental challenges related to the social determinants of health. Reading to children promotes language and social development and promotes long term literacy and educational attainment. At a Canadian women and family focused interdisciplinary HIV clinic with many vulnerable families, an evidence based literacy program was implemented in January 2013. The components are pediatrician counseling on literacy promotion at most pediatric visits, provision of free books and having a volunteer reader to role model and read with children in the waiting room.

Methods: A brief quality improvement survey to assess the perceived value of "Read to Succeed" was administered to a convenience sample of 28 families with children aged 0-18 years and 16 of 25 clinic staff (clinical, clerical and research staff).

Results: After two years of the program, 28 families were interviewed with a total of 51 children aged 6 weeks to 16 years old. 13% of parents reported that their own literacy was too poor to be able to read with their children. Half were reading more than once weekly with their children. Only 32% of children had seen the reading volunteer. 68% of families reported taking books home; 11% reported reading more often because of the free books. All families indicated that they wished the program to continue.

Literacy program awareness was high amongst staff (88%) and 100% of those surveyed indicated that the program should continue. The majority of the 16 clinicians (81%) reported speaking with families about literacy. Staff suggested having a greater variety of language and cultural books (French, aboriginal and African stories), and increasing volunteer hours.

Conclusions: Pediatrician counseling and provision of free books can promote language and literacy development; a literacy intervention in an HIV clinic is well liked by both families and staff.

CSP6.07

HIV Exposed, but Uninfected Infants: Missed Opportunities for Early Developmental Services from a Canadian Tertiary Care Centre

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Background: HIV uninfected children born to HIV-positive mothers (HIV exposed uninfected infants, HEU) are at risk for adverse developmental outcomes. Evidence shows that social determinants of health play a larger role than does HIV. Developmental screening and early referral may improve outcomes.

Methods*:* A retrospective chart review of all HEU born in British Columbia between January 1, 2008 and June 30, 2013 was done as a quality assurance study. We examined developmental screening, referrals, and referral completion in a provincial family-centered HIV clinic caring for 20-30 HEU newborns/year and identified barriers to referral completion.

Results: We reviewed 112 subjects: 64 (57%) male; 87 (77%) born at term (>37 weeks). In addition to the mother being HIV+, 78 (66%) were from socially vulnerable families (parental ill health, parental addictions, poverty, limited literacy, limited English language skills, etc), including 43 (38%) who had some involvement with child protection services. 104 (92.8%) had at least one documented standardized developmental assessment. Forty-six (44.2%) children were noted to have a developmental concern at some point, and of those, 40 (87.0%) were referred on. 43 referrals were made to developmental service providers; 58.1% of referred children had been seen and of those, 60% had reports sent to the clinic. Of 36 referrals to general pediatricians, 69.4% had occurred, 92.0% of whom communicated recommendations back to the clinic. Barriers to referral completion included inability to contact caregivers (7.3%), patient no-show (13.0%), waiting lists (23.2%), and other (56.5%).

Conclusion: Patients were screened and referred appropriately, but many either were not assessed or no information was communicated back to the clinic. HEU families had particular difficulty accessing developmental services because of both systematic issues (wait lists, confusing system) and family issues (no phone, difficult to contact, moving frequently.) Future work will examine how to overcome these barriers.

HIV in Vulnerable Populations and Global Health Issues
Le VIH dans les populations vulnérables et les enjeux sanitaires mondiaux

CSP7.01

Characteristics of HIV-Positive Patients Requiring Salvage Therapy in Downtown Vancouver, BC

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Background: Historically, patients who have received multiple antiretroviral regimens have been placed on more complex regimens termed "salvage therapy." These regimens are often multi-class, multi-tablet regimens with issues of drug interactions, side effects, and reduced adherence. In order to determine which salvage therapies will be most effective among current treatment options, it would be useful to better characterize the population being considered for such interventions

Methods: We have evaluated 81 HIV-positive patients who have received >2 antiretroviral treatment regimens and who were seen at a tertiary clinic in the inner city of Vancouver. Data were abstracted from regular medical follow up visits, including demographic information.

Results: A total of 81 subjects (15.4% of the overall clinic population having been seen quarterly over the past year) required salvage therapy, with a median 3 (3-13) prior antiretroviral treatment regimens. The median age was 52 (32-81) years, 29 (35.8%) of whom were people who inject drugs (PWID), 44 (54.3%) identified as men who have sex with men (MSM), 32 (39.5%) co-infected with HCV, and 11 (13.6%) on opiate substitution therapy. This is representative of the overall clinic population except for an over-representation of MSM. The most common salvage regimen was Stribild with or without darunavir (15), with other regimens being Atripla (5) and Complera (4). After a median follow-up of 25 months, 90.1% have achieved virologic suppression (VL<400 copies/mL). Of 8 who have not, their major characteristics are 4 (50.0%) MSM and 6 (66.7%) PWID.

Conclusion: Salvage therapy accounts for about 10-15% of a large clinic population, with an over-representation of MSM, likely related to a longer period of engagement in care in this population. Such regimens that historically included up to 10 agents are now remarkably simple and effective given currently available options that have combined multiple agents into a single tablet.

CSP7.02

Factors Leading to Regimen Change in HIV-Positive Patients

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Background: HIV-infected individuals are often prescribed multiple antiretroviral regimens before successfully achieving virologic suppression. Developing a clearer understanding of factors that contribute to regimen change will allow physicians to manage this process more efficiently, especially in more vulnerable populations, where data on this issue are lacking.

Methods: We have evaluated 125 HIV-positive patients who required a regimen change within the last 12 months and who were seen at a tertiary clinic providing multidisciplinary care to patients living in the inner city of Vancouver. Data were abstracted from regular medical follow up visits, including demographic information and the specific justification for a regimen change.

Results: In total, of 523 evaluated subjects, 125 (23.9%) required a regimen change within the last 12 months. Of these, 112 (89.6%), a proportion consistent with the general clinic patient population, were male, with 61 (48.8%) identified as men who have sex with men (MSM) and 53 (42.4%) were people who inject drugs (PWID). The mean age was 49.2 (22-81) years and 53 (42.4%) were co-infected with HCV. The reasons for a regimen change were side effects (25.6%), simplification or issues of adherence (18.4%), virologic failure (12.0%), desire to enroll in a clinical trial (14.4%), and preparation for HCV treatment (6.4%). Changes included a change in NRTI backbone (80), initiation of an integrase inhibitor (52) and initiation of a single-tablet regimen (53). In follow-up of 12 weeks, virologic suppression (VL <400 copies/mL) was observed in 85% cases, including 87% switched for virologic failure.

Conclusion: Changes in antiretroviral therapy remain quite common for a variety of clinical indications. Virologic failure is still relatively common, perhaps more so in inner city vulnerable populations such as ours. The variety of current treatment options allows for changes to be made in a way that generally achieves and maintains virologic suppression.

CSP7.03

Impact of Short-Term Incarceration on HIV Outcomes

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During incarceration, the opportunity can be taken to engage human immunodeficiency virus (HIV) positive prisoners with chaotic lifestyles into care. Previous studies show an association with improved antiretroviral therapy (ART) adherence and immunologic and virologic outcomes during incarceration, although these gains are often lost upon release into the community. However, the impact of short-term incarceration in a Canadian context of universal health coverage has not been previously reported and could have significant implications in optimizing HIV patient outcomes given the large number of HIV positive patients cycling through short-term remand centres. The objective of this study was to assess the impact of short-term incarceration on ART adherence, virologic suppression and enrolment into community care post release amongst HIV patients.

We conducted a retrospective cohort study of patients who attended the HIV Outreach Clinic at a Canadian remand centre between September 2007 and December 2011 to assess the impact of short-term incarceration on ART adherence, virologic suppression and enrolment into community care post release. Outpatient enrolment increased significantly (53% (95%CI: 40.0-67.0) to 76.0% (95%CI: 65.0-87.0, p=0.01)) as did ART adherence (55.2% to 70.7% (p=0.01)) post-incarceration. Although not significant, there was a trend towards improved virologic suppression (less than 40 copies/ml; 50% to 77.8% (p= 0.08)) post incarceration and 70.4% of patients sustained supression one-year post-incarceration (p =0.70). Our study suggests that short-term incarceration provides an opportunity to optimize HIV patient outcomes; however, further interventions are needed to sustain these benefits post-release.

CSP7.04

Characteristics of HIV Positive Patients Who Were Lost to Follow-Up in the Inner City

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Introduction: Patients infected with HCV and/or HIV are often marginalized and have many vulnerabilities, precluding ongoing engagement in health care. Although we have developed a novel multi-disciplinary model of care to address this challenge, a proportion of patients are still lost to follow-up (LTF). We have conducted a retrospective study to evaluate the characteristics of such patients, with a view to designing interventions to enhance retention in long-term follow-up.

Methods: A retrospective chart review was undertaken of all HIV-infected patients followed at the Vancouver Infectious Diseases Clinic. LTF was defined as no clinic visits occurring over the past 12 months. We collected information related to demographic, behavioral and medical variables with a view to identify characteristics associated with retention in long-term medical care.

Results: A total of 517 individuals were evaluated, 77 (14.9%) of whom were LTF. Within this group, (mean age 49.2 years), there were 83.3% male, 33.8% people who inject drugs (PWID), 55.8% MSM, 88.3% on antiretroviral

therapy, 38.9% co-infected with HCV, and 5.2% on methadone.

Discussion: Within our diverse cohort of HIV-infected individuals receiving care within our multi-disciplinary clinic, HCV co-infection and methadone maintenance therapy were found to be protective with respect to LTF. These are markers of enhanced engagement in multiple aspects of service offered in our centre. Going forward, we will test the hypothesis that enrollment in multiple aspects of our program (meeting a broader range of patient needs) will help reduce the proportion of patients who are lost to ongoing HIV care.

HIV in Women and in Pregnancy
Le VIH chez les femmes et pendant la grossesse

CSP8.01

Attitudes and Practices of Canadian Healthcare Providers on Breastfeeding by HIV-Infected Women

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Background: Breastfeeding by HIV-positive women in Canada has serious clinical, psychosocial, medicolegal and public health implications. The purpose of this survey was to assess attitudes and practices of Canadian healthcare workers (HCWs) on this topic.

Methods: The survey was developed in expert consultation and distributed using REDCap to Canadian HCW (HIV providers (HIVP), General Infectious Disease-Microbiology (ID/M) providers, and Community Pediatrics (CP)). Questions on attitudes toward medicolegal aspects, clinical management, and resource utilization were asked using 3 and 5 point Likert rating scales, multiple choice questions, and scenario based questions. Standard descriptive and bivariate statistics were used.

Results: 152 responses were received (HIVP=104; ID/M=21; CP=27). HIVP included nurses (48%), physicians (26%), pharmacists (24%), and social workers (4%), whereas ID/M and CP were all physicians. For the cohort as a whole, breastfeeding by HIV-positive women was considered criminal always/sometimes (32%), warranting Child Welfare Service involvement always/sometimes (76%) and warranting Public Health involvement always/sometimes (90%). HIV was regarded as an absolute contraindication to breastfeeding by 51% (HIVP=46%, ID/M=57%, CP=41%). HIVP were less likely to support routine Public Health referral (HIVP=27%, ID/M=100%, CP=54%; p<0.001) and were more likely than CP to support free formula for all breastfeeding women (HIV=84%, ID/M=76%, CP=52%, p<0.01). 52% of HCWs indicated that recommending breastfeeding in Canada would only be acceptable if the risk of transmission was zero; 31% indicated that a risk of <1% would suffice and 8% said it should be the mother's choice regardless of risk.

Conclusions: For the most part the attitudes and practices of HIV, ID/M and CP providers regarding breastfeeding by HIV infected mothers were similar. A substantial minority were accepting of the possibility of breastfeeding by HIV-positive women despite some risk of HIV transmission. Taken together, these findings suggest that further discourse in this area is needed.

CSP8.02

Canadian Health Care Provider Knowledge on Breastfeeding by HIV-Infected Women

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Background: The World Health Organization (WHO) recommends exclusive breastfeeding by HIV-positive mothers in resource-limited settings and exclusive formula feeding in resource-rich settings. This dichotomy is often confusing in a real world setting, which is highly transnational. Anecdotal evidence suggests many healthcare workers (HCWs) are not fully aware of or are confused by current guidelines or science that informs them. The objective of this survey was to assess the knowledge of Canadian HCWs regarding breastfeeding by HIV-positive mothers.

Methods: The survey was developed in expert consultation and distributed using REDCap to three HCW groups (HIV providers (HIVP), General Infectious Disease-Microbiology providers (ID/M), and Community Pediatrics (CP)). Knowledge was tested using multiple-choice questions on current guidelines, infant-feeding terminology and HIV transmission concepts. Standard descriptive and bivariate statistics were used.

Results: In total, 152 responded (HIVP n=104; ID/Micro n=21; CP n=27). HIVP included nurses (48%), physicians (26%), pharmacists (24%), and social workers (4%), whereas ID/M and CP were all physicians. HIVP were of similar age, but more likely to be female (Fisher's exact=83.3, df=86, p<0.001). HIVP exhibited better knowledge with respect to the risk of breastmilk transmission of HIV while on combination antiretroviral therapy (HIV=58%, ID/M=42%, CP=25%; Chi-sq 7.7, df=2, p=0.02), the meaning of exclusive breastfeeding (HIV=93%, ID/M=74%, CP=84%; Fisher's exact=6.51, df=2, p=0.027), understanding that transmission risk is highest with mixed feeding (HIV=69%, ID/M=70%, CP=17% Chi-sq=21.67, df=2, p<0.001), and awareness of provincially-sponsored formula programs

(HIV=74%, ID/M=60%, CP=37%, Fisher's exact=14.78, df=6, p=0.012). Awareness and knowledge of the WHO and Canadian recommendations did not differ (ANOVA p=0.596 and p=0.097, respectively).

Conclusions: This survey demonstrated a higher knowledge level among HIV care-providers in Canada with respect to infant feeding, however gaps remain among all three groups. Areas identified for ongoing improvement include knowledge related to current guidelines, transmission risk, and availability of infant-feeding resources in Canada.

CSP8.03

Key Interventions and Populations to Target to Facilitate ART Use: Findings from the Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS)

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Objectives: To estimate the proportion of Canadian women living with HIV who are not currently on antiretroviral therapy (ART) overall according to key socio-demographic, psychosocial and clinical characteristics.

Methods: We analysed baseline survey data from the Canadian HIV Women's Sexual and Reproductive Health cohort study (CHIWOS), a longitudinal multi-site, community-based research study of 1,425 women with HIV from British Columbia, Ontario and Quebec. The primary outcome was self-reported use of ART (Yes vs. No); women with missing information were excluded (n=41). Descriptive and standard bivariable statistics were used to describe and compare the probability of not currently using ART. Multivariable logistic regression was used to identify independent correlates of previous ART use status among women not currently on ART.

Results: A minority of women (12.1%, 168/1384) was not currently on ART. Of these, 67 (39.9%) reported an undetectable VL with a median CD4 count of 769 cells/mm^3; while 101 (60.1%) reported a VL>50 copies/mL with a median CD4 count of 500 cells/mm^3. In multivariable analysis, the odds of never being on ART were significantly higher among women with a history of incarceration in the past year (aOR=2.25; 95%CI=0.44-11.58; p-value=0.023) or previous but not current injection drug use (IDU) (aOR=2.95; 95%CI=0.85-10.23; p-value=0.010) and lower among women with more children (aOR=0.51 per additional child; 95%CI=0.36-0.72, p-value=<0.001) or a history of depression (aOR=0.95; 95%CI=0.90-0.99, p-value=0.05).

Conclusions: Among the small proportion (12.1%) of women not currently on ART, some were likely elite controllers, long-term non-progressors, and women not started on ART due to high CD4 counts. HIV care provider education focused on updated ART initiation guidelines may be required. Incarceration or IDU were risk factors for never being on ART. This suggets that social support and addiction treatment interventions may hold promise for promotion of ART use among women.

CSP8.04

A Message from MoM: Anti-Oppressive Approaches to Clinical HIV Care Throughout Pregnancy, Birth and Motherhood

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Introduction: There is a lack of knowledge about how pregnancy experiences for women living with HIV (WLHIV) are unique, particularly those who may be demographically similar. This abstract highlights similarities and differences in these experiences and provides implications for clinical practice when caring for pregnant WLHIV.

Methods: The Mothering on the Margins (MoM) study followed HIV-negative participants (N=30) who were matched to WLHIV in the HIV Mothering Study (HMS). Matching criteria included age, race, place of birth, and current city. Corresponding to the HMS design, narrative interviews were conducted in the third trimester, and at 3 and 12 months postpartum. Analysis of the third trimester narratives was conducted with academic and community-based researchers and compared with third trimester narratives of HMS participants.

Findings: Commonalities between narratives included fears and anxieties, often related to fetal well-being, prenatal health, and motherhood. Anxieties were also expressed about negotiating disempowering relationships with healthcare providers, where concerns/fears were dismissed and silenced. Discussions about social support were also common, although availability was individualized. A layer of uniqueness became evident for WLHIV that is associated with HIV status, including HIV related stigma, disclosure of HIV, and concerns about surveillance of their infant feeding practices.

Implications: Findings from the HMS suggest that WLHIV experience a higher degree of stigma and surveillance during pregnancy. While this message is consistent with clinical observations, the MoM study is the first to substantiate this finding. Clinical implications of this study are rooted in how this message informs practice. While the common narratives can be used to support the 'normalization' of pregnancy for WLHIV, unique experiences must also inform care. An anti-oppressive approach may help to address the clinical and support needs of WLHIV by considering ways in which care can better attend to the experiences of WLHIV that remain rooted in HIV-stigma.

HIV Prevention
Prévention du VIH

CSP9.01

Reducing Risk of HIV Transmission among Gay and Other Men Who Have Sex With Men in Smaller Urban Settings Requires Greater Attention to Their Mental Health

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Introduction: HIV transmission among gay and other men who have sex with men (GMSM) is consistently high in Canada, and GMSM experience higher rates of depression and anxiety compared to the general population. We hypothesized this may be more significant in small-medium sized urban settings where GMSM are less visible and have more difficulty accessing culturally appropriate care.

Methods: A survey of GMSM living in the Ottawa area was conducted. The survey was accessible online and in paper format and was promoted through community and professional organizations, the Sexual Health Centre, social media, and online sex websites. Data were compiled and analyzed using SPSS software.

Results: Whereas GMSM account for 54.3% of new HIV infections in Canada in 2014, they account for 77% of new infections in Ottawa in the same time period. Importantly, 31% of GMSM in Ottawa reported a diagnosis of depression and/or anxiety, far above the 4.7% point prevalence in the general population and among GMSM in large urban areas (17.2% in San Francisco, New York, Los Angeles and Chicago). In addition, 45% live to some degree "in the closet," a factor contributing to poor mental health, and 25% found sex causes them to feel stressed or anxious at least half the time.

Discussion: These data suggest men living in small-medium sized urban settings suffer greater mental health challenges and account for a higher proportion of HIV infections. In order to address HIV transmission and improve the overall health of GMSM, we suggest greater attention to the mental health needs of these men, including innovative approaches to identify men at-risk, removing stigmatizing barriers, and improving accessibility to culturally appropriate mental health services.

CSP9.02

Adherence counseling in a community-based setting for daily oral TDF/FTC-based HIV pre-exposure prophylaxis (PrEP)

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Background: Adherence is the primary determinant of efficacy for daily PrEP. We describe our experience providing adherence counseling in a community-based setting to participants in Canada's first PrEP demonstration project.

Methods: Participants in the PREPARATORY-5 study underwent a one-on-one adherence support session at a randomly assigned timepoint during the trial. The intervention was adapted from the Next Step Counseling PrEP adherence support strategy developed specifically for use with MSM, and was delivered by an AIDS Committee of Toronto counselor. Session notes and participant evaluation form were summarized using content analysis and descriptive statistics.

Results: 42/52 participants have completed counseling sessions. Most (59.5%) had never spoken to a counselor about HIV-related issues before. Participants reported that they felt listened to and understood (100%), that they were treated with confidentiality and respect (97.6%), and that they had the right amount of time with the counselor (100%). Most would recommend such sessions to other PrEP users (97.6%), and found the session helpful (95.2%), although existing self-reported adherence was high. Common facilitators of adherence were: a greater sense of control over sexual health (n=33), anxiety reduction (n=31), and already established routines (n=26), while interruption of routine (n=7), lack of easy access to medication (n=6), and chaotic lifestyles (n=6) were common barriers. Five participants identified specific adherence-related needs, related to adherence during routine interruption and/or when socializing. Five participants identified a new adherence strategy, all of whom were able to successfully implement it at 2-3 week follow-up. Many participants valued the opportunity to discuss their PrEP experience outside the clinic setting.

Conclusions: Although most participants had no adherence challenges, most valued the opportunity to discuss

PrEP and sexual health in a supportive environment. Future analyses will evaluate the impact of the intervention on PrEP adherence, as measured by self-report, pill-count and intra-erythrocyte tenofovir disphosphate levels.

CSP9.03

Recruitment of Healthy Kenyan Women into the KAVI-VZV 001 Study: a Trial Designed to Characterize Mucosal Immune Responses Induced by VZV Vaccination

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Background: An HIV vaccine able to induce a durable immunity ready to contain HIV at its early stages of infection is our best hope for ending the AIDS epidemic. We hypothesize that Varicella Zoster virus (VZV) is a promising vector for HIV antigens because it generates effector memory, which does not require priming allowing an immediate response to incoming virus at the mucosa. Our preliminary results in cynomolgus macaques supports this hypothesis. In an attempt to move towards a VZV-based HIV vaccine we are characterizing the mucosal immune activation and effector immunity induced by VZV vaccination. The collection of mucosal sampling, especially rectal biopsies, can pose a challenge to such studies. In this trial we are enrolling healthy Kenyan women willing to undergo repeated mucosal sampling.

Methods: Recruitment includes: i) Community Meetings – informing potential participants of the study at KAVI; ii) Pre-Screenings – up to 3 visits detailing the study objectives, requirements and implications to each volunteer; and iii) Clinical and Laboratory Screenings to assess volunteer's eligibility.

Results: The study is currently ongoing. To date we have recruited 13 of the 44 women we target for this study. We have observed that less than 25% of the volunteers referred by the community leaders reach the screening phase. Approximately 55% of the volunteers are lost between Community and Pre-screening II. Among the screened subjects, 50% were eligible to enroll. Primarily, the causes for ineligibility were: persistent bacterial vaginosis, Hepatitis C, VZV naïve, no compliance with an effective contraceptive method, and pregnancy.

Perspectives: This study will help to assess VZV as a potential vector for an HIV vaccine, to identify the main challenges in conducting mucosal studies and set the ground for vaccine trials involving mucosal sampling.

CSP9.04

HIV-1 Infection With Multi-class Resistance Despite Pre-Exposure Prophylaxis (PrEP)

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Background: PrEP is reported to have nearly 100% prevention efficacy in men who have sex with men (MSM) with optimal adherence. We report a 43 year old MSM who seroconverted to multi-class resistant HIV-1 after 24 months of successful PrEP (4th generation Ag/Ab combo screen reactive, p24 reactive, Western Blot non-reactive on day 0), despite clinical and pharmacokinetic data suggesting long-term adherence to FTC/TDF.

Methods: Pharmacy dispensing records were obtained. Liquid chromatography–mass spectrometry (LC-MS) was performed on untimed plasma from day 0 to determine TDF and FTC concentrations. Dried blood spots (DBS) were collected on day 16, while on FTC/TDF-based combination antiretroviral therapy, for determination of intracellular TVF-DP concentration. Standard sequencing, deep sequencing phenotypic testing for resistance to integrase inhibitors, and phylogenetic analysis of the V3 loop of gp120 were completed on day 7 plasma (HIV RNA 28,326 copies/mL).

Results: Pharmacy records demonstrated consistent prescription refills. DBS testing revealed TVF-DP of 2,297 fmol/punch indicating consistent dose-taking in the preceding 1-2 months, thus overlapping with the seroconversion time. LC-MS on day 0 plasma was inconclusive for TDF (calibration range 181-2,385 ng/ml) and FTC (range 736-50,200 ng/ml) due to the untimed nature of the sample relative to dosing and the high lower limit of quantification of the assay. Standard and deep sequencing revealed CCR5-tropic clade B HIV-1 with mutations conferring resistance to NRTIs (41L, 67G, 69D, 70R, 184V, 215E), NNRTIs (181C) and INSTIs (51Y, 92Q), suggesting transmitted resistance. Phenotypic drug resistance testing of the integrase class revealed reduced response to all integrase inhibitors. Phylogenetic analysis demonstrated infection from a single source.

Conclusion: This patient's clinical history, pharmacy records and DBS results consistent with long-term dosing of FTC/TDF suggest that HIV infection is possible despite adherence to daily oral PrEP when exposed to FTC/TDF-resistant virus.

Mental Health Issues for HIV Positive Persons
Questions de santé mentale pour les personnes séropositives au VIH

CSP10.01

Health service outcomes among persons with HIV following a mental health admission: a population-based study

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Background: Persons with HIV in Ontario have rates of mental health illness that are approximately 2-fold higher than those of the general population. However, there are no studies examining outcomes of persons with HIV following a hospitalization for mental health illness. Accordingly, we compared health service outcomes among persons with and without HIV following a mental health admission between January 1, 2006 and December 31, 2013.

Methods: We conducted a population-based study using Ontario's health administrative databases. We used Cox proportional hazard models to compare the cumulative incidence of readmission to a mental health bed, mental-health related emergency department visits and outpatient psychiatry visits 90 days following discharge from a designated mental health bed, between persons with and without HIV.

Results: During the study period, 980 persons with HIV and 251,323 HIV-negative adults were hospitalized with a mental health illness. Compared with HIV-negative individuals, persons with HIV were predominantly male [78.4% vs. 50.2%; standardized difference (SD) = 0.56] and more likely to be admitted for a substance use disorder (31.4% vs. 16.2%; SD = 0.24). Following multivariable adjustment, there was no difference in rates of readmission [hazard ratio (HR) 0.90; 95% confidence interval (CI) 0.76 to 1.07), mental health related emergency department visits (HR 0.92; 95% CI 0.79 to 1.07) or outpatient psychiatry visits (HR 0.92; 95% CI 0.84 to 1.01). Stratification by sex did not change the results appreciably. Prior mental health diagnoses were associated with readmission and emergency room use.

Conclusion: Mental health related health service outcomes are similar among persons with and without HIV discharged from a mental health bed in Ontario. Our results underscore the importance of optimizing the management of mental health illness for all individuals, irrespective of HIV status.

Pharmacology, Pharmacokinetics and Pharmacoeconomics
Pharmacologie, pharmacocinétique et pharmacoéconomie

CSP11.01

Nevirapine Pharmacokinetics in HIV-exposed Neonates Receiving Triple Combination Antiretroviral Therapy as Post-Exposure Prophylaxis

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Background: Neonates at increased risk of HIV infection receive treatment dose nevirapine (NVP)-based triple combination antiretroviral therapy (cART) as HIV-post exposure prophylaxis (HIV-PEP) at our centers. We evaluated the pharmacokinetics (PK) and safety of this dosing regimen.

Methods: Neonates given NVP-based cART HIV-PEP between September 2012 and April 2015 were prospectively enrolled after obtaining informed consent. Retrospective data for infants who received cART HIV-PEP prior to this period were also included. NVP was dosed at 150 mg/m^2 daily x 14 days, then twice daily x 14 days, with levels pre-dose at weeks 1 and 2, and pre-dose and 1 and 4 hours post-dose at week 4. Dosing was adjusted if trough levels (NVP-T) fell outside the therapeutic range (3-8 mg/L).

Results: NVP-Ts was obtained for 34 infants (15 prospective). Median gestational age (GA) and birth weight (BW) were 37 weeks (30-41) and 2.9 kg (1.05-4.18), respectively. Median NVP-T was 8.3 mg/L (1.6-25.4 mg/L) and 3.7 mg/L (1.6-26.1 mg/L) at week-1 and -2, respectively. The proportion of therapeutic NVP-T increased from 36% (9/25) at week-1, to 54.5% (12/22) at week-2 and 73.9% (17/23) at week-4. Supra-therapeutic NVP-T's were observed in 56% (14/25) and 9.1% (2/22) at week-1 and -2, respectively. Median oral clearance (ClssF) increased from 0.054 L/kg/hr (0.011-0.499) to 0.168 L/kg/hr (0.005-0.777) while median drug exposure (AUCt) decreased from 168.3 mg/L*hr (20.0-844) to 50.43 mg/L*hr (1.31-1206.86). Higher AUCt correlated with younger GA (r=0.523, p=0.003) and lower BW (r=0.432, p=0.015). The most common adverse events were asymptomatic laboratory abnormalities including hyperlactatemia (22.7%), anemia (19.3%), and neutropenia (18.2%). Rash occurred in 3.4% and transaminitis in 2.2%.

Conclusions: Treatment dose NVP was well-tolerated. Drug clearance increased with maturity but most infants

did not have therapeutic levels initially. Lower empiric dosing with therapeutic drug monitoring may be required for low BW or premature infants.

CSP11.02

Escalating Doses of Levothyroxine due to a Probable Drug Interaction in a Patient Receiving a Ritonavir-Boosted HIV Protease Inhibitor Regimen

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Objective: To describe a case of an HIV-infected patient with hypothyroidism whose thyroid function did not normalize despite escalating doses of levothyroxine.

Methods: Case report.

Case: A 37-year-old HIV-positive African female who had undergone thyroidectomy to treat a benign multinodular goiter was found to be hypothyroid. Levothyroxine 75 mcg daily was initiated. While treated with abacavir/lamivudine (600/300 mg tablets) and lopinavir/ritonavir (800/200 mg tablets) the patient's thyroid stimulating hormone (TSH) remained elevated (up to 125.89 mIU/L, reference range 0.30-6.0 mIU/L) despite daily doses of levothyroxine titrated to 175 mcg. An interaction between ritonavir and levothyroxine via a ritonavir-mediated induction of levothyroxine glucuronidation was suspected to be the cause of the ongoing TSH elevation, and lopinavir/ritonavir was substituted with dolutegravir 50 mg once daily. Within 4 months, the TSH had normalized to 0.12 mIU/L with a free T4 of 16.1 pmol/L (reference range 9.0-23 pmol/L). Based on TSH concentrations, the levothyroxine dose was gradually tapered down over a 7-month period and stabilized at a dose of 125 mcg daily. The TSH remained within the normal range after a 9 month follow-up period on the same dose of levothyroxine. To assess the probability of a causal relationship, the Drug Interaction Probability Scale (DIPS) was applied and scored this interaction as probable (score = 8/11).

Conclusion: This case highlights a potentially serious and under-recognized drug interaction between ritonavir and levothyroxine. Based on this case and a review of other cases reported in the literature, the dose of levothyroxine might need to be more than doubled to effectively treat patients who are taking ritonavir concurrently. However, upward titration of levothyroxine doses may be insufficient to normalize thyroid function. To avoid the ritonavir-levothyroxine interaction, ritonavir can be replaced with an agent that does not interact with levothyroxine.

CSP11.03

Lack of Drug Interactions between Tenofovir Alafenamide-based Antiretroviral Single Tablet Regimens and anti-HCV Single Tablet Regimen Ledipasvir/Sofosbuvir

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Introduction: Use of anti-HCV agents such as ledipasvir (LDV), a P-glycoprotein (Pgp) inhibitor, with HIV antiretrovirals (ARV) such as tenofovir alafenamide (TAF), a Pgp substrate, may be complicated by drug-drug interactions (DDIs). Two Phase 1 studies evaluated DDIs between TAF-based regimens rilpivirine (RPV; R)/emtricitabine (FTC; F)/TAF or elvitegravir/cobicistat/ FTC/TAF (E/C/F/TAF) and fixed-dose combination anti-HCV LDV/sofosbuvir (SOF).

Methods: In two multiple-dose, randomized, crossover studies, healthy volunteers received R/F/TAF (25/200/25 mg) [Study 1] or E/C/F/TAF (150/150/200/10 mg) [Study 2]), alone or in combination with LDV/SOF, daily with food for 11 [Study 1] or 10 [Study 2] days. Plasma concentrations of RPV, EVG, COBI, FTC, TAF and TFV (TAF metabolite), LDV, SOF and GS-331007 (SOF metabolite) were analyzed and PK parameters calculated via noncompartmental analysis. Geometric least squares mean ratio (GMR; combination vs. alone) and 90% confidence intervals (CI) for analytes' AUC, C_{max} and C_{tau} were estimated by linear mixed effect modeling and compared to lack of alteration bounds (70-143% except RPV: 80-125%). Safety was assessed throughout the studies.

Results: Forty of 42 subjects (Study 1) and 30/30 subjects (Study 2) completed study. Treatments were generally well tolerated. GLSM and 90% CIs for all analytes were contained within the prespecified bounds except TFV when RPV/FTC/TAF was administered with LDV/SOF, COBI, when E/C/F/TAF was coadministered with LDV/SOV, and LDV and SOF when administered with E/C/F/TAF.

Conclusions: Despite increase in TFV exposure upon coadministration of R/F/TAF + LDV/SOF, the mean TFV AUC_{tau} is ~ 5 times lower than TFV from TDF, and within the range of TFV that did not lead to renal AEs or bone loss. There is no association between higher COBI exposure and incidence of AEs, renal function parameters. Exposures of LDV and SOF, while higher, are in the exposure-safety range. R/F/TAF or E/C/F/TAF may be coadministered with LDV/SOF without dose modification.

CSP11.04

Development of an HIV and Hepatitis C Drug Therapy/ Drug Interaction Application

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Purpose: Antiretrovirals (ARVs) and directly acting antivirals (DAAs) for hepatitis C (HCV) continue to be developed and marketed at a rapid pace. There is a high potential for drug interactions with these medications, particularly in patients with high rates of comorbidities, polypharmacy, and coinfection. Specialized drug interaction applications tend to focus on either HIV or HCV therapies, but not both in an integrated program. An HIV/HCV pharmacology and drug interaction application was developed in order to assist practitioners managing these complex patients, and to promote safe and rational prescribing.

Methods: The application development team consists of 3 pharmacists, two computer programmers/developers and a medical interface designer. ARV and DAA information from two existing, internationally recognized websites, www.hivclinic.ca and www.hcvdruginfo.ca was updated and consolidated into a drug database. The web application allows users to search for ARV or DAA drug information, and to quickly check for drug interactions involving ARVs and/or DAAs with other drug classes using an interactive search engine.

Results: The web application includes information on 45 HIV and HCV licensed and investigational drugs and allows for interaction searches with over 500 other commonly prescribed drugs. The database is regularly updated to include the latest publications and presentations from major HIV and HCV scientific conferences, and currently includes interaction information on over 15,000 unique drug combinations. The application is available on the HIV & HCV websites, which receive over 2000 separate visits per month. A free mobile native application will soon be available for download from the websites and from iTunes/ Google Play stores in order to reach a vastly greater audience.

Conclusions: This web application consolidates ARV and DAA information from two established, internationally recognized drug therapy websites into a single program, and allows practitioners to quickly identify and manage significant drug interactions in HIV and/or HCV-infected patients.

CSP11.05

A probable drug interaction between lurasidone and atazanavir-based antiretroviral therapy: a case report

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Introduction: Lurasidone, an atypical antipsychotic for schizophrenia and bipolar-I associated depression, achieves its effects via antagonism of dopamine (D_2) receptors in the mesolimbic and mesocortical pathways. Likewise, it also produces extrapyramidal effects through blockade of dopamine in the nigrostriatal pathway. Motor side effects include dystonia, parkinsonism and tardive dyskinesia. Lurasidone is primarily metabolized by CYP3A4 isoenzyme. Protease inhibitors, such as atazanavir, may precipitate drug interactions via CYP3A4 inhibition. We report the first case in which co-administration of these medications resulted in clinically significant adverse effects.

Case Summary: A 63 year-old HIV-positive male patient presented to hospital after a fall. Physical exam showed worsening tremor, cogwheeling, and new onset shuffling gait. Other pertinent conditions include schizoaffective disorder for which he received lurasidone 40mg daily, risperidone 1mg daily, divalproex 1000mg twice daily, benztropine 2mg twice daily, and lorazepam 2mg nightly. Antiretroviral regimen included abacavir/lamivudine/ zidovudine 300/150/300mg twice daily, atazanavir 400mg daily, dolutegravir 50mg daily, and rilpivirine 25mg daily. Other medications include bezafibrate, rosuvastatin, ezetimibe, and melatonin. Risperidone was discontinued but extrapyramidal effects paradoxically worsened. Plasma 2-hour peak lurasidone concentration drawn was 100ng/ mL. Antiretroviral regimen was modified to avoid inhibition of CYP3A4 by atazanavir. After 4 weeks on a new antiretroviral regimen with tenofovir/emtricitabine/rilpivirine 300/200/25mg daily and dolutegravir 50mg daily, repeat peak lurasidone plasma concentration was 24ng/mL at the same dose. This correlated with decreased muscle rigidity and return of his gait to baseline, while maintaining control of his schizoaffective disorder.

Summary: This combination should be used with caution, based on the findings in this patient. When concomitant use of lurasidone and atazanavir is required, we propose using the lowest effective dose of lurasidone, monitoring for adverse effects clinically, and considering measurement of serum drug concentrations. The case highlights the vulnerability to polypharmacy and adverse drug events in HIV-positive patients with concurrent psychiatric disease.

Resistance
Résistance

CSP12.01

HyDRA -- A novel bioinformatics tool for next generation sequencing-based HIV drug resistance data analysis

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Background: Monitoring of HIV drug resistance (DR) is essential in effective HIV/AIDS management at both individual and population levels. Conventional HIV DR assays rely on bulk sequencing of HIV samples, usually present as quasispecies, which are limited by their ability to identify low-abundance drug resistant variants (LADRVs) present at frequencies below 20% in the viral population. Next generation sequencing (NGS) technologies, such as the Illumina MiSeq, effectively address the LADRV issue through massive clonal sequencing of input templates. However, the requirements for high throughput computing and sophisticated bioinformatics strategies in NGS data analysis are impediments to adopting NGS in research and clinical HIV DR monitoring as well as large scale surveillance testing.

Methods and Results: To facilitate NGS-based HIV DR data processing, HyDRA, a custom HIV drug resistance analysis pipeline has been developed, along with HyDRA Web a full featured web application. HyDRA was developed in Perl and leverages existing open source bioinformatics software, such as Bowtie2, for reference mapping. It carries out the multi-step data processing starting from raw NGS data input (in .fastq *or .sff* formats) through to customizable reporting on HIV DRM at a full range of frequencies, including LADRVs. HyDRA Web was designed for users with minimal bioinformatics experience and enables remote users without computational capacity to perform HyDRA analyses with ease. By producing a consensus sequence at user-defined threshold for minor variant detection, HyDRA also supports "one sample, one sequence" analysis which can approximate and substitute conventional genotypic HIV DR assays if required.

Conclusion: HyDRA automates NGS-based HIV DR analysis and is accessible via internet for any authorized end-users. As NGS trends to become the primary HIV DR testing technology, HyDRA has the potential to be applied in any laboratories performing NGS-based HIV DR typing or investigating LADRVs for clinical monitoring or surveillance purposes.

CSP12.02

Simplification of Antiretroviral Therapy to Stribild/ Darunavir in Treatment-Experienced HIV Positive Patients: a Case Series

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Background: Long term survivors of HIV infection often have a history of multiple antiretroviral (ARV) regimens consisting of complex dosing schedules and pill burdens, frequently required to overcome varying degrees of ARV drug resistance. For simplification, convenience, and improved adherence, a switch to a once-daily, two-tablet schedule of Stribild® (STR) [tenofovir/emtricitabine/elvitegravir/ cobicistat] plus darunavir (DRV) may offer a novel regimen in this group.

Objective: To describe the simplification to STR/DRV in treatment-experienced patients with respect to virologic and immunologic response, pill burden, and dosing frequency.

Methods: This was a case series conducted at an ambulatory HIV clinic in Windsor, ON between November 2013 and December 2014. Treatment-experienced patients simplified to STR/DRV during the study period were included. Patient demographics, virologic and immunologic responses, drug resistant mutations, change in pill burden and dosing frequency were summarized.

Results: Of the 7 patients evaluated, the median age was 52 (35-64). All had a CD4 nadir of <200 cells/mm^3, with a median duration of HIV infection of 18 (14-28) years. Median baseline CD4-cell count was 461 (116-588) cells/mm^3. At the time of simplification, 4 patients had undetectable viral loads (VL), 2 had VL <250 copies/mL, and 1 had a VL of 36,746 copies/mL. Patients had a median of 6 (1-13) prior regimens and 6 (4-7) daily ARV pills prior to simplification. Six patients had likely or confirmed TAMs, 5 had likely or confirmed M184V, and 1 had DRV RAM. None had K65R or INSTI resistance. Median follow up was 13 (6-17) months, during which all patients sustained immunologic response and achieved or maintained virologic suppression.

Conclusion: The combination of STR/DRV appears to be an effective and simple option for treatment-experienced patients. Additional prospective studies evaluating the clinical efficacy, therapeutic drug monitoring, patient satisfaction and tolerability may give clinicians greater confidence in its utility.

CSP12.03

Genotypic and phenotypic drug resistance of Human Immunodeficiency Virus type 1 strains to Reverse Transcriptase Inhibitors in Suzhou, China

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Objective: After 30 years of 7 same antiretroviral drugs being repeatedly used in China, it is now important to find out the drug susceptibility and resistance of the circulating HIV-1 strains in the country. This study is to investigate the genotypic and phenotypic drug resistance of HIV-1 strains to a variety of used and non-used NRTI and NNRTI drugs in Suzhou, China.

Methods: HIV-1 RT genes from 19 treatment-naïve or –experienced HIV patients in Suzhou, China, were PCR amplified and sequenced for genotypic analysis, and the resulting RT fragments were then cloned into a NL4-3 vector through a yeast-based cloning system to produce infectious viruses for phenotypic drug resistance assay with 8 NRTI and 5 NNRTI drugs, including the 6 RTI drugs being currently used in China.

Results: Sequencing analysis showed that 6 out of 19 patients were HIV-1 clade B, 5 were CRF01AE, and 8 were CRF01AE/B. For the six RTI drugs currently used in China, almost all of the 19 HIV-1 strains showed drug resistance against AZT and TDF to various degree, >63% were resistant to EFV and 3TC, and 42.1% resistant to NVP, with the only exception of D4T (only one resistant strain). The genotypic analysis showed that the most common resistant mutation in these HIV-1 strains were K43E (11/19), I135V/T (6/19), K238R (12/19) and A371V (13/19), and the less frequent resistant mutations were V118I (3/19), V179I (3/19), E203D (4/19), Q278E (3/19) with the rare resistant mutations of V106I, D218N, K219T, and A288T. Interestingly, the strain RT45 with D218N and K219T showed the broadest resistance against 9 different RTI drugs, including all of the six received and 3 non-received drugs.

Conclusions: This study revealed that the circulating HIV-1 strains have developed severe drug resistance against most the antiretroviral drugs currently applied in China.

CSP12.04

Tenofovir and Emtricitabine Resistance in the CANOC Collaboration: Implications for PrEP

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Introduction: The real-world effectiveness of tenofovir (TDF)/emtricitabine (FTC) containing regimens as HIV pre-exposure prophylaxis (PrEP) may be limited in settings of high levels of baseline resistance to these drugs.

Methods: We determined the prevalence of TDF and FTC resistance among patients enrolled in the Canadian Observational Cohort (CANOC), an interprovincial collaboration of 8 cohorts of antiretroviral naïve HIV-positive individuals who initiated combination antiretroviral therapy (cART) after January 1, 2000. Prevalence of TDF and FTC resistance was determined prior to ARV initiation and during follow-up among patients with virologic failure (1000 copies/mL at least 6 months after cART initiation). Resistance data were obtained from routine clinical population viral sequence data, and interpreted using inferred phenotypes.

Results: Resistance data were available for 4512 (82%) of 5495 patients. Resistance status was available at ARV initiation for 3760 (68%) patients and 4996 follow-up resistance tests were obtained for 1919 (35%) patients. Prior to cART initiation, there were 3 (0.1%) patients with resistance to TDF, 58 (1.5%) with intermediate susceptibility to TDF, and 25 (0.7%) with resistance to FTC. Of the 1911 patients experiencing virologic failure, 1358 (71%) patients had follow-up resistance data available and 24 (1.77%), 59 (4.34%) and 337 (25%) harboured resistance to TDF, had intermediate susceptibility to TDF, or harboured resistance to FTC, respectively. Assuming that rates of resistance were equivalent among patients who were eligible for resistance testing, the estimated rates of resistance to TDF, intermediate susceptibility to TDF and resistance to FTC among participants on cART would be 0.06%, 1.5% and 8.5% during the study period.

Conclusion: There were very low levels of resistance detected among ARV naive patients. Resistance to components of Truvada, and FTC in particular, was present in a substantial number of patients with virologic failure capable of transmitting HIV which might impact the efficacy of PrEP.

Substance Use and HIV
Toxicomanies et VIH

CSP13.01

A Latent Class Analysis of Substance Use Patterns Among Canadian Women Living with HIV: Implications for Improving Health Equity by Addressing Social Determinants

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Background: Substance use has multiple health consequences for women living with HIV (WLWH). We analyzed substance use patterns among Canadian WLWH to determine the effects of substance use on cART adherence and identify social determinants of health covariates.

Methods: Survey data were analyzed for 1,363 WLWH in the Canadian HIV Women's Sexual and Reproductive Health Cohort Study. We used latent class analysis to model patterns of current substance use based on seven individual (alcohol, tobacco, cannabis) and grouped (recreational drugs, misused prescription drugs, stimulants, opiates) indicators, measured as any use v. no use. Fit statistics indicated best class solution. Multinomial logistic regression with class membership as the dependent variable identified independent covariates.

Results: We found 6 latent classes: Abstainers (26.3%); Tobacco Users (8.8%); Alcohol Users (31.9%); Tobacco, Alcohol, and Cannabis Users (13.9%); Users of Non-Illicit and *Some* Illicit Drugs (recreational, stimulants) (9.8%); Users of Non-Illicit and *All* Illicit Drugs (9.3%). Among those currently taking cART, 73.4% were >=95% adherent. Bivariable analyses revealed significantly increasing proportions of Indigenous women and sexual minorities, and decreasing incomes, resiliency scores and adherence with each subsequent class. Results were mirrored in multivariable analyses. Women identifying as Indigenous v. Caucasian (AOR: 1.71 (95% CI: 0.88, 3.32)) and LGBTQ v. heterosexual (2.24 (1.09, 4.6)) as well as those with resiliency scores < median (2.41 (1.37, 4.22)), incomes <$20,000 (3.6 (1.78, 7.28)), and **adherence <95% (2.41 (1.37, 4.22))** were more likely to be Users of Non-Illicit and *All* Illicit Drugs than Abstainers.

Discussion: Findings indicate heterogeneity in substance use patterns among WLWH. Latent classes with increasing numbers of drugs used were associated with lower cART adherence and increased societal marginalization. To improve adherence and associated benefits, programs must ally with WLWH to transform the social systems and conditions that threaten their health and everyday lives.

CSP13.02

Morbidity and Mortality Among HIV-Infected Substance Users in Manitoba

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Background: Substance use is common amongst HIV-infected individuals in Manitoba and leads to poor patient outcomes. This study aims to describe the comorbidity and age of mortality of HIV-infected substance users in Manitoba.

Methods: Clinical records of 564 HIV-infected individuals in care at Health Sciences Centre in Winnipeg, Manitoba were reviewed. Clinical data were extracted from patient charts for all patients identified as substance users (illicit substance users, alcohol abusers and chronic users of opioids or benzodiazepines) and non-users. Age of mortality at one year following the initial chart review was recorded for both substance users and non-users.

Results: Among 215 HIV-infected substance users in Manitoba, 49% had been previously diagnosed with an Axis 1 psychiatric disorder. Substance users diagnosed with an Axis 1 disorder were significantly more likely to have used benzodiazepines than substance users without psychiatric illness. Since their initial presentation, 14%, 12% and 2% of substance users had been diagnosed with chlamydia, gonorrhoea and syphilis, respectively. Among substance users, 20 had been diagnosed with active tuberculosis while 8 had been diagnosed with latent tuberculosis. Hepatitis B and C co-infection were present in 4% and 36% of substance users, respectively. Substance users were significantly more likely to have abnormally elevated liver enzymes than non-substance users. A significant difference in age of mortality was found between substance users and non-users with users dying nearly 20 years earlier than non-users.

Discussion: Comorbidity is common among HIV-infected substance users in Manitoba including mental illness and co-infections. Substance users are also at risk of dyeing at a younger age than non-users. A holistic, patient-centred approach to care is crucial in treating HIV-infected patients who use substances in order to reduce comorbidity and mortality.

CSP13.03

Characteristics of women living with HIV who use illicit drugs and experience incarceration in a Canadian setting

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Background: Women who use drugs are overrepresented among female inmates in Canadian correctional facilities. We sought to identify factors independently associated with incarceration among women living with HIV (WLWH) who use drugs in British Columbia.

Methods: We used longitudinal data from the AIDS Care Cohort to Evaluate Survival Services (ACCESS), a cohort of people living with HIV who have used illicit drugs in Vancouver, linked to longitudinal clinical data. Female participants completing semi-annual study interviews between September 2005-May 2014 were included. The primary outcome was self-reported incarceration in the six months before a study visit. We used generalized estimating equations to identify factors independently associated with incarceration.

Results: Of 847 ACCESS participants, 285 women were included. Median participant age at study baseline was 40 (Interquartile range [IQR]: 33-46), and median number of study visits per participant was 9 (IQR: 4-12). During the study period, 86 women (30%) reported ≥1 incarceration event. Among those incarcerated, the median number of incarceration events was 1 (IQR: 1-2). Factors independently associated with incarceration included recent homelessness (AOR: 2.44, 95%CI: 1.57-3.77), heroin injection (AOR: 2.35, 95%CI: 1.51-3.65), and syringe lending (AOR: 4.54, 95%CI: 1.45-14.23). Women who were older at study baseline (AOR: 0.97, 95%CI: 0.94-0.99), and achieved HIV viral suppression (AOR: 0.56, 95%CI: 0.33-0.96) were less likely to experience incarceration.

Conclusions: Almost one third of WLWH in this cohort experienced incarceration during the study period. Incarceration was independently associated with periods of homelessness and viral detectability among these women. Due to poor continuity of care between community and correctional healthcare services, incarceration may represent an additional barrier to healthcare engagement of marginalized WLWH. Improved linkage to HIV, housing and addiction services in the community is indicated to advance the clinical and risk profile of WLWH at risk of incarceration, combined with women-centred prison outreach programs.

CSP13.04

Stribild: a Promising New Treatment for Suppression of HIV Viral Load in People Who Inject Drugs

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Background: Single tablet regimens have been shown to be highly effective in clinical trials of initial antiretroviral therapy, as well as in patients requesting treatment simplification. Their efficacy in people who inject drugs (PWID) has been less specifically evaluated as such patients have been largely excluded from participation in clinical trials.

Methods: We have established a multi-disciplinary program to recruit and retain HIV-infected PWID in care. Antiretroviral (ARV) treatment is offered to all who qualify for it. Data were abstracted from regular medical follow up visits. This analysis has focused on the evaluation of the virologic response to Stribild as a single tablet, as administered to PWID.

Results: Within our active cohort of 537 HIV-infected patients, 182 are PWID (actively using a median of 3 recreational drugs) on active ARV treatment, 20 on Stribild for a median 461 (310-895) days. Key characteristics include: 80% male, 35% heroin use, 50% stimulant use, 55% on opiate substitution therapy. Of 162 on other regimens for median of 602 (73-891) days, characteristics are: 82% male, 17% heroin use, 32% stimulant use, 35% on opiate substitution therapy. In the Stribild group, 11 received treatment as part of initial engagement in care, while 9 switched from a previously effective regimen. In median follow-up of 16 months, virologic suppression (VL <400 counts/mL) was achieved and maintained in 16 patients, including 7/9 with previous virologic suppression. This compares to 78% efficacy in all ARV regimens administered to PWID in our centre.

Conclusion: Newer single tablet regimens such as Stribild have yet to be used extensively in HIV-infected PWID. They appear to be safe and effective either as initial or switch therapy. Longer-term follow-up in larger PWID populations is indicated to better inform the use of this important therapeutic modality in vulnerable populations.

Clinical Sciences Other
Sciences cliniques, Autre

CSP14.01

HIV-Specific Patient-Reported Outcome Measures: A Scoping Review of Available Tools in 2015

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Background: Greater use of patient-reported outcome (PRO) measures to provide feedback to health profession-

als could improve HIV care and patient satisfaction and lead to more patient-centered care. In HIV, while PROs are used in research, their application in clinical practice is at an early stage relative to other specialties. Many issues must be addressed when considering their implementation, including PRO selection. Because past reviews of PROs in HIV have concerned particular areas (e.g., disability), a more comprehensive and updated review of available PROs in HIV is needed, in part, to facilitate their consideration. Our objective was to conduct a scoping review of PROs designed for use with HIV-positive persons to create a repertoire of such measures and to assess their range and concentrations.

Methods: We searched 8 electronic databases for eligible English or French language PROs (Sept 24 2014-Oct 7 2015). Content analysis helped to generate a classification framework for the HIV-specific PROs retained.

Results: Our search identified 2,875 records of which 92 instruments met our criteria and were classified in our repertoire. The greatest concentrations of measures were in the categories of Health-related quality of life (HRQL) (24%) and Resilience (23%). Next most common were measures concerned with Medication (17%), followed by those focused on Symptoms (10%), Negative psychological impacts (9%) and Healthcare evaluation (8%). Fewer tools were oriented to Stigma (6%) and Body issues (3%).

Discussion: Our classification challenges understandings of PROs as largely concerned with HRQL, underscoring a variety of HIV-specific instruments, including many devoted to the personal and social resources of people living with HIV (Resilience). It also points to the interest of further PRO development in such areas as healthcare evaluation, patient-identified medication adherence barriers and sexual health in HIV. Finally, our repertoire offers a resource for the HIV field to consider further PRO application.

CSP14.02

Patterns of Physical Activity and Associations with Metabolic Health in Men Living with HIV Compared to Age Matched Controls

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Introduction: Physical activity has known benefits for those living with HIV, and is an independent predictor of the metabolic syndrome among people living with HIV. Despite this, few studies have objectively measure the physical activity patterns, or examined the relationship between physical activity and indices of metabolic health among those living with HIV. The primary aim of this study was to objectively measure physical activity levels among men living with HIV and to compare this to a population of age matched HIV-negative men. It was also an aim to compare physical activity levels with public physical activity recommendations. A secondary objective was to investigate the association between indices of metabolic health and physical activity levels.

Methods: Twenty men living with HIV and twenty age-matched men were recruited and consented to take part in this study. Due to unforeseen circumstances data analysis was conducted on 38 men (19 in each group). Physical activity was measured using the actigraph accelerometer and was supplemented with activity diaries. Venous blood samples (insulin resistance, total cholesterol, triglycerides, and both low and high density lipoprotein cholesterol) were measured by routine laboratory methods.

Results: Men with HIV were significantly more physically active than their non-HIV infected peers, and were reaching public physical activity guidelines. Significant inverse correlations between moderate physical activity and both insulin resistance (ρ -0.847; $p<0.001$) and triglycerides (ρ -0.575; $p=0.013$) as well as moderate to vigorous physical activity (MVPA) with both insulin resistance (ρ -0.785; $p<0.001$) and triglycerides (ρ -0.484; $p=0.042$) were seen in those living with HIV only.

Conclusion: Results of this study show that men with HIV can and are achieving public physical activity guidelines. Results also emphasize the importance of physical activity in reducing the risk of the metabolic syndrome and cardiometabolic diseases in men living with HIV.

CSP14.03

The effects of a 16 week aerobic exercise programme on cognitive function in people living with HIV

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Since the introduction of highly active antiretroviral therapy there has been a marked increase in the prevalence of HIV associated neurocognitive disorders. It has been suggested that higher levels of physical fitness are associated with higher levels of cognitive function in people living with HIV. This project aimed to investigate whether a 16 week exercise intervention could improve cognitive function in people with HIV. Thirteen participants were recruited from a pre-defined group of patients previously screened for cognitive impairment. The participants were randomised into an exercise group (n=6) that completed a 16 week supervised aerobic exercise programme training 2 to 3 times per week, and a control group (n=7) that received routine care. Primary outcomes measured included cognitive function (Montreal Cognitive Assessment, and the trail making tests A and B), aerobic fitness (Modified Bruce Protocol), sleep quality (Pittsburgh Sleep Quality Index), metabolic profiles and anthropometrics. Pearson or Spearman's rank correlation coefficients were uesd for baseline analysis where appropriate. Two way repeated measures ANOVA was used to compare physiological and performance variables. Effect sizes were calculated using Cohen's *d*. Higher levels of moderate physical activ-

ity and aerobic fitness were significantly correlated with higher cognitive function at baseline (P=0.04 and P=0.006 respectively). There was a tendency for a numerically larger improvement in short term memory in the exercise group compared to the control group (effect size of 0.67 vs 0.56). However, there were no significant improvements in global cognitive scores. Significant improvements were seen in daytime dysfunction, which describes daytime energy levels and ability to complete daily tasks, in the exercise group following training compared to the control group (P<0.05). In conclusion exercise may have beneficial effects on cognitive function and sleep quality in people with HIV. Further research in this area is required.

CSP14.04

Characteristics of Persons Living with HIV attending Self-Management Programs offered in the Manitoba HIV Program

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Background: Nine Circles Community Health Centre (NCCHC), the primary care site of the Manitoba HIV Program (MHP), offers two types of self-management programs to People living with HIV (PLWH). *Living Well with HIV* (LWH) was developed by NCCHC as an introductory program to improve participant's understanding of HIV. *Get Better Together!* (GBT) is a licensed version of the Chronic Disease Self-Management Program (CDSMP) developed by the Patient Education Research Centre at Stanford University. GBT is a generic program that aims to develop participant's capacity in managing their chronic condition(s) and overall health. Both programs are available to PLWH who receive care at either the primary or tertiary care site of the MHP.

Objectives To describe the characteristics of PLWH accessing self-management programs and to identify gaps and opportunities to enhance self-management programs offered through the MHP.

Study design: Retrospective descriptive study based on chart audit.

Results: Between April 1, 2014 and December 31, 2015, 8 self-management courses were offered at NCCHC (4 LWH courses consisting of 3-6 weekly sessions; 4 GBT courses consisting of 6 weekly sessions). The number of registrants for each LWH and GBT course was similar (4-9 registrants per course). 30 PLWH attended at least one LWH session; 15 PLWH attended at least one GBT session. We will present socio-demographic characteristics and clinical indicators, including CD4 and viral load, of self-management participants during this time period.

Conclusions: The MHP offers HIV-specific and general chronic disease self-management programming. Engagement in self-management programming is higher for patients who receive care at the primary care site where programming is offered. Future research/evaluation projects could be aimed at identifying point(s) along the HIV care continuum at which patients are engaging with self-management programming, and assessing whether certain clinical outcomes could be used as indicators to evaluate the effectiveness of these programs.

CSP14.05

Blood-Brain Barrier Dysfunction as a Novel Biomarker and Therapeutic Target for HIV-Associated Neurocognitive Disorders

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Background: HIV-associated neurocognitive disorders (HAND) remains a highly prevalent and significant public health concern. The neuropathogenesis of HAND is presumed to result from complex interactions between viral replication within the central nervous system (CNS), immune response, brain inflammation and neurotoxicity. Accumulating evidence indicate a key role for blood-brain barrier (BBB) dysfunction in the pathogenesis of a number of common CNS disorders. BBB dysfunction is a common finding in HIV infected individuals and the severity of neurocognitive impairment was found to be correlated with BBB permeability. Animal studies show that long-lasting BBB dysfunction underlies inflammatory transforming growth factor beta (TGF-β) signaling and neural dysfunction. To quantitatively evaluate BBB pathology, we developed a computational approach for contrast-enhanced magnetic resonance imaging (CE-MRI) and demonstrated that blocking TGF-β signaling in rodents prevents BBB-mediated cerebral dysfunction, endorsed BBB closure and halted neuronal damage.

Methods<: A retrospective clinical validation pilot-study for detection and quantification of brain vessel pathology in patients with HAND. Sequential MRI scans of patients with HAND were retrieved and analyzed for presence of BBB alterations and correlation with associated neuropsychiatric complications.

Findings: In comparison to healthy brain tissue, contrast-enhanced T1-weighted images showed areas with abnormal BBB permeability. Increased signal and pathological BBB were correlated with prominent neurocognitive deterioration and reduced signal and pathological BBB were correlated with neurological improvement.

Conclusion: The compelling causal link between BBB impairments and neural dysfunction and degeneration highlights vascular integrity as a target for early diagnosis and treatment of HAND. Quantitative MRI assessment of brain vessel permeability can identify and characterize subjects at-risk and may lead to the use of BBB imaging as a biomarker for treatment consideration, specific neurotherapeutic target and a potential predictor of patients' outcome.

CSP14.06

The impact of the episodic nature of chronic illness: a comparison of Fibromyalgia, Multiple Sclerosis and Human Immunodeficiency Virus (HIV)

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Purpose: To understand the episodic nature of HIV and compare characteristics of HIV to other chronic illnesses including multiple sclerosis (MS), and fibromyalgia (FM).

Method: We conducted a narrative review of literature that described the characteristics of individuals living with HIV, MS and FM. Searches were performed in electronic databases (PubMed, OVID, CINHAL and Google Scholar) using a combination of keywords including episodic, relapse, remission, fluctuation. Articles published between 2004-2014, that described health challenges and episodic nature of illness were included. Data were extracted from selected articles, including the authors, date of publication, study population, the aims of the study, outcome measures and main study findings. These were charted and collated to the dimensions of disability in the Episodic Disability Framework.

Results: Forty seven articles were included. The comparison of HIV with MS and FM demonstrated the similarities and differences in the nature of disability experienced specifically, physical, cognitive, mental and emotional symptoms, difficulties in daily functioning, challenges to social inclusion and uncertainty. Fluctuations in health were identified among the three chronic conditions. Distinct features of HIV included HIV stigma and discrimination, concurrent health conditions, side effects of medication and aging with HIV that influenced the episodic nature and uncertainty.

Conclusions: In summary, people living with HIV experience common issues of episodic illness similar to those experienced by people with MS or FM. These similarities may not be exclusive to these three chronic illnesses, and could apply to individuals living with other chronic illnesses that are episodic. Using the broad context of episodic disability could bring more episodic health conditions together to jointly pursue issues related to access rehabilitation services that may be used to help address disability and improve overall health of people with HIV and other episodic illnesses.

Epidemiology and Public Health

Épidémiologie et santé publique

Data Science, Data Visualization and Big Data in Public Health Research
Science des données, visualisation des données et mégadonnées dans la recherche en santé publique

EPHP1.01

#PrEP @ #CROI2015: Exploring the roles of Twitter user types in sharing and discussing new evidence on HIV pre-exposure prophylaxis (PrEP)

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Background: Government and non-government organizations (GOs/NGOs) use social media to share/start conversations about new HIV information. We used Twitter and the release of new PrEP evidence at CROI 2015 as a case study to explore the role of different user types on social media, paying specific attention to opinion leaders (OL).

Method: PrEP/CROI related terms were used to extract English language tweets posted from February 8th to April 5th, 2015 (CROI: February 26-29). We defined tweets with ≥1 retweet as being an OL tweet, and used a coding guide to characterize these tweets. Tweets were coded as being informational (e.g., relaying or providing information about PrEP) or conversational (e.g., comments/opinions, campaigns, advocacy). We used regression analyses to identify characteristics associated with retweet number.

Results: Our data extract included 7,902 PrEP-related tweets; 21.5% were OL of which 805 were coded at random. OL tweets were from unaffiliated individuals (28.7%), NGOs (27.1%) and GOs (1.5%), broadcast media (21.4%), Twitterbots (11.2%) and social media/blogs (5.1%). Tweet

volume was highest during CROI and overall 53.3% of tweets were CROI-related. Most tweets were informational (65.0%); these tweets dominated during CROI with an increasing proportion of conversational tweets thereafter. Conversational tweets were most common among unaffiliated individuals (47.6%) and social media/blogs (51.2%) followed by GOs/NGOs (35.4%), broadcast media (30.2%), and Twitterbots (2.2%). After adjusting for other characteristics, retweet number was not associated with content (informational vs. conversational, p=0.3) but was higher during CROI, and for GOs/NGOs and broadcast media compared with unaffiliated individuals.

Discussion: PrEP evidence released at CROI was shared rapidly on Twitter leading to social media conversations over the subsequent six weeks. In our preliminary analysis, findings differed by user type with NGOs contributing a quarter of all tweets in our sample suggesting an important role in sharing/starting conversations about new HIV information online.

Demography of HIV and Estimates of Key Population Sizes
Démographie du VIH et estimations de la taille des populations clés

EPHP2.01

Assessing Injection Drug Use from Diagnostic Codes in Administrative Healthcare Data: the British Columbia Hepatitis Testers Cohort

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Large linked administrative datasets "big data" are being used to track progress and effectiveness of hepatitis C (HCV) and HIV programs. People who inject drugs (PWID) are an HCV/HIV priority population; however, diagnostic codes do not differentiate non-injection from injection drug use (IDU). We assessed the validity of diagnostic code algorithms in identifying IDU against interview data.

The British Columbia Hepatitis Testers Cohort (BC-HTC) includes 1,417,780 individuals tested for HCV, HIV or reported as a case of HBV, HCV, HIV or tuberculosis in BC from 1990-2013, linked to administrative datasets including physician, hospitalization and drug dispensation data. A subset was interviewed at the time of HIV or acute HCV/HBV diagnosis about risk factors including injection drug use (n=8,240). ICD-9/ICD-10 codes for illicit drug use, opioid substitution therapy (OST) and injection-related infections were reviewed and grouped into multiple IDU indicators. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated. Indicators were applied to the overall BC-HTC cohort to estimate PWID population size.

A combination of broad drug misuse and OST codes had the highest sensitivity and lowest specificity (88.2/64.3; PPV 51.3; NPV 92.7) while an algorithm including only injectable drugs and injection-related infections within one year of drug use had the lowest sensitivity and highest specificity (55.6/84.6; PPV 60.6; NPV 81.7). Intermediate between these, the optimal combination identifying PWID focused on injectables and did not require injection-related infection (81.5/71.6; PPV 55.2; NPV 88.6). Based on this definition, in the BC-HTC, 79,139 had a history of injecting drugs prior to 2013 and 25,054 were injecting in 2010-12.

Identifying PWID using diagnostic codes in big data is crucial for tracking the progress of programing aimed at PWID throughout the cascade of care. With population-based datasets, this tool can be used to inform much needed estimates of PWID population size.

EPHP2.02

HIV Incidence among MSM Attendees of Sexually Transmitted Infection Clinics across British Columbia, Canada

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Background: Identifying risk groups of MSM with the highest HIV incidence rates is important to determine those who may be prioritized for targeted prevention interventions such as HIV pre-exposure prophylaxis.

Methods: Data from a clinical electronic charting system at 15 STI clinics in BC from 2000-2013 were extracted for clients identifying as MSM. Incident cases were defined as testers who had ≥1 HIV- test and a subsequent HIV+ test. Overall incidence and rates were analyzed using multivariate binomial regression with a person-year offset. Rates associated with high-risk behaviors and ever having other STIs were calculated.

Results: There were 204 seroconverters among 6,088 HIV testers who contributed 19,868 person-years to the analysis for an overall incidence rate was 1.0/100 person-years (95% CI: 0.9-1.2). The median age was 33 years (IQR: 27-42) and clients had a median number of 1 test (IQR: 1-3). Incidence rates were higher for clients: 15-19 years of age (3.8/100 person-years; 1.2-8.7); with ≥15 partners in the previous 6 months (1.6/100 person-years; 0.8.0-2.8); who reported inconsistent condom use (1.7/100 person-years; 1.3-2.0) vs. consistent; who reported HIV-positive partners (2.0/100 person-years; 1.0-3.5), and who ever had a diagnosis of rectal gonorrhea (4.6/100 person-years; 3.5-

5.8), syphilis (3.6/100 person-years; 2.5-4.9), or chlamydia (1.6/100 person-years; 1.3-2.1). Clients presenting with two risk factors had significantly higher incidence rates; e.g., rectal gonorrhea and syphilis diagnoses (17.0/100 person-years (10.4-25.6)) and rectal gonorrhea diagnosis and inconsistent condom use (8.3/100 person-years (5.6-11.7)). After accounting for variation in testing rates and incidence trends over time, the multivariable model showed that ever having syphilis, ever having rectal gonorrhea, and inconsistent condom use were independently associated with increased probability of seroconversion.

Conclusion: MSM with other STI diagnoses and inconsistent condom-use had very high rates of HIV incidence. These groups should be engaged in additional HIV prevention interventions.

Economic Evaluation of Policies, Programs or Interventions
Évaluation économique des politiques, des programmes ou des interventions

EPHP3.01

The Need for Compassionate Supply of Antiretroviral Medications Provided Through the Manitoba HIV Program: A Retrospective Review

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Background: Antiretroviral medications are the cornerstone of HIV therapy, however the ability to access antiretroviral medications can be challenging without universal drug coverage. The Manitoba HIV Program provides HIV care to approximately 1200 people living with HIV in Manitoba; a portion of who have significant barriers to accessing antiretroviral medications despite the availability of a variety of publicly funded drug insurance programs. The goal for providing compassionate supply of antiretrovirals is to prevent delays in treatment initiation and interruption of chronic treatment.

Objectives:

1. To determine the incidence of patients requiring a compassionate supply of HIV medications.
2. To quantify the amount of compassionate antiretroviral medications provided over 1 year.
3. To identify the barriers and challenges that patients encountered that prevented them from obtaining antiretrovirals through publicly funded programs.

Methods: A retrospective chart review of patients who received a compassionate supply of HIV medications though the Manitoba HIV Program (Health Sciences Centre and Nine Circles Community Health Centre) over 1 year (January 1, 2015 to December 31, 2015) will be conducted. Patient demographics, current drug coverage, duration and quantity of compassionate supply and challenges to obtaining HIV medications through publicly funded programs will be collected.

Results: Results will be presented after completion of chart review and analysis. The results of the study will be important for programs in order to provide supports and to assist policy makers to understand the implications and obstacles patients encounter with the current publicly funded programs.

EPHP3.02

In What Circumstances Could Non-daily Pre-exposure Prophylaxis (PrEP) Substantially Reduce Program Costs (HPTN 067)?

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Background: Pre-exposure prophylaxis (PrEP) reduces HIV acquisition risk if patients adhere sufficiently. Non-daily PrEP based on potential HIV exposures is expected to require fewer pills than daily PrEP, reducing costs. We estimated cost reductions for non-daily PrEP for different populations.

Methods: We estimated the required number of PrEP pills/person/week for three PrEP dosing regimens used according to protocol in the HPTN 067/ADAPT trial (daily, time-driven (two pills/week 3-4 days apart & one pill within 2h after sexual intercourse), and event-driven (pills taken 24-48h before & within 2h after sexual intercourse)), for different sexual behaviour patterns (number & spacing of sex-days/week). Using trial data and behavioural and cost (drug and non-drug costs) data obtained through systematic literature reviews, we estimated cost savings due to pill reductions for non-daily versus daily PrEP, under ideal conditions of 100% adherence.

Results: Per protocol, for 1, 2, 3 and 4 sex-days/week, 2, 3–4, 4–5 and 5–6 pills/week respectively were required with event-driven, and 2–3, 2–4, 3–5 and 5–7 pills/week for time-driven, vs. 7 pills/week for daily PrEP. Across populations from HPTN 067/ADAPT, and other trial and real-world populations identified in the literature review, the median number of sex-days varied between 1–3/week. Drug costs reviewed accounted for 82–96% of PrEP program costs in high-income countries, but as little as 35–53% in some low-resourced countries. Program costs were reduced the

most in settings where drug costs accounted for the majority of program costs, and in populations with low sexual activity, e.g. by 64–69% with event-driven PrEP for low-activity (1 sex-day/week) U.S. populations.

Conclusion: Non-daily PrEP could cost substantially (>50%) less than daily PrEP in populations with low sexual activity in high-income countries, if taken as prescribed. The next step is to combine cost and effectiveness estimates (considering actual adherence) to evaluate the overall cost-effectiveness of non-daily PrEP.

Epidemiology and Surveillance of HIV Co-infections
Épidémiologie et surveillance des coinfections au VIH

EPHP4.01

HCV Re-Infection in High-Risk HIV Co-Infected People Who Inject Drugs in a Multidisciplinary Clinic

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Background: People who inject drugs (PWID) constitute the majority of cases of HCV infection in Canada and many of them are also co-infected with HIV. Although a number of strategies have been developed to engage them in care, reluctance to implement them relates at least in part to concerns about re-infection following successful HCV treatment. We have examined this issue in a prospective longitudinal cohort to establish whether this concern is confirmed in clinical practice. A multidisciplinary approach to treat HCV in PWID co-infected with HIV can help to avoid recurrent HCV viremia.

Methods: Within a multidisciplinary program to engage and treat PWID, we have documented 45 cases of HCV therapy in HIV infected individuals having resulted in a sustained virologic response (SVR) in which patients continued to engage in high-risk behaviour for HCV acquisition after SVR was achieved. These individuals have been followed prospectively to document recurrent viremia, with the performance of HCV RNA testing every 6 months, more frequently if elevated ALT or symptoms of acute hepatitis were noted. The endpoint of this analysis is a positive HCV RNA test following the clear establishment of an SVR.

Results: Among the 45 HIV and HCV co-infected patients, who were treated for HCV and achieved SVR, a mean age was 52.8 years, 7.6% were females. Of these patients, 62.9% had genotype 1, and 92.5% were previously treatment naïve. In a mean of 5.95 person-years of follow-up/subject, 0 cases of HCV re-infection were noted.

Conclusion: In our cohort, HIV co-infected PWID successfully treated for HCV infection do not experience HCV re-infection as previously encountered in uninfected at-risk individuals. The risk of HCV re-infection in co-infected individuals receiving care in multidisciplinary programs is very low. HIV infection is not a risk factor for recurrent HCV viremia.

EPHP4.02

Characterization of HCV Infected PWID in the Setting of Clinical Care in Canada (CAPICA): A retrospective study

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Background: HCV-related liver disease in people who inject drugs (PWID) carries a heavy healthcare and societal burden. Current HCV treatment uptake in PWIDs is low and related to barriers at the individual, provider and healthcare system levels. Data regarding HCV PWID already engaged in care may provide insights into treatment barriers; this information could be used to develop targeted medical and psychosocial interventions.

Aims: In this observational study, we intend to describe HCV disease in PWIDs currently followed in Canadian clinics. Study site characteristics, demographics, substance abuse, co-morbidities, HCV disease, HCV treatment history and use of opiate substitution therapy (OST) were captured.

Methods: A multicenter, retrospective, database/chart review was performed to collect and summarize data on 450 patients from twelve centers across Canada. Subjects receiving medical care, with chronic HCV infection, and a history of injection drug use (in the past 12 months) were included. Patients with HIV co-infection were excluded.

Results: Preliminary data (185/450 patients): 68.1% were male, 75.1% Caucasian and 14.6% Aboriginal. The median age was 40 (18-63) years. 36.8% of patients were known to participate in a needle exchange program, 24.9% have been or were currently being treated for HCV, of which 69.6% were treated with a regimen containing pegylated interferon and 4.8% of the patients were re-infected after achieving a sustained virologic response (SVR). Patients were not treated for the following reasons: 56.1% were not ready, 23.0% had mild liver disease, 6.5% because of co-morbidities, 5.0% for unwillingness, and 9.3% for unknown reasons or missing information.

Conclusions: This study will allow us to better characterize HCV infection in PWIDs currently engaged in care in Canada. This information will help optimize protocols for HCV treatment in this important population.

EPHP4.03

Trends in causes of mortality in the Canadian Co-infection cohort (CCC) 2005 – 2015

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Previous analysis of the Canadian Co-infection Cohort identified end-stage liver disease (ESLD) as the primary cause of death. As the cohort ages, other comorbidities may become prominent. We reviewed trends in cause-specific mortality over time.

Data were analyzed from participants followed January 2005 to May 2015. All reported deaths were classified following the "Coding of Death in HIV" (CoDe) system. Event rates per 1000 person-years for the early (2005 – 2010) and late cohort periods (2010 – present) stratified by age (20 – 50, > 50) were calculated. Comparison of trends between early/late periods was performed using Poisson regression, 95% confidence intervals were constructed using the normal approximation for the log rate ratio.

Overall 1296 participants (73% male) contributed 5480 person-years of follow-up, of whom 178 died. Causes of death could be assigned in 138 participants. The mortality rate [95% CI] for period 1 was 26.22 [19.61, 35.05] per 1000 person-years (PY) and 24.72 [20.17, 30.3] per 1000 PY. Overall ESLD rates declined from 8.16 [4.84, 13.76]/1000 PY to 6.91 [4.71, 10.15]/1000 PY, overdose-death rates declined from 6.99 [3.97, 12.31]/1000 PY to 3.19 [1.81, 5.63]/1000 PY and cancer rates dropped from 4.66 [2.34, 9.3]/1000 PY to 3.46 [2.01, 5.95]/1000 PY from period 1 to period 2. Deaths from cardiovascular disease appeared to increase from 1.75 [0.56, 5.42] to 2.66 [1.43, 4.94] /1000 PY. ESLD was the most common cause of death overall; principally among those >50 years (14.62 [3.88, 55.24] and 10.34 [4.3, 24.8]/1000 PY for periods 1, 2 respectively, whereas for those < 50 there were slightly more overdose deaths.

Overall mortality rates have not increased over time, but differ by age. End-stage liver disease deaths have declined, however still remain the primary cause of death in the cohort, highlighting the need for wider uptake of HCV therapy.

EPHP4.04

Characteristics of a Core Group of Gay, Bisexual and Men Who Have Sex with Men (MSM) with ≥4 Infectious Syphilis Infections in British Columbia (BC) from 2005 to 2014

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Background: The rate of syphilis has increased in BC, from 6.8 to 11.9 per 100,000 from 2005 to 2014. Small subpopulations are disproportionately burdened by syphilis. We sought to characterize the socio-demographics, partner notification outcomes and social network of a core group with ≥4 infectious syphilis diagnoses in BC from 2005-2014.

Methods: An STI clinic chart review was conducted for each individual with ≥4 syphilis infections between 1/1/2005 and 31/12/2014, identified through the provincial STI surveillance database. Descriptive statistics of the age, gender, ethnicity, exposure category, stage of infection, HIV status at diagnoses, number of contacts and partner notification outcomes was completed, along with a social networking analysis (SNA).

Results: Between 2005-2014, there were 30 individuals with ≥4 syphilis diagnoses, accounting for 139 diagnoses. All were MSM, 24 (80%) self-reported as Caucasian and 29 (96%) were HIV positive at their last syphilis diagnosis (1 of the 29 seroconverted during the study period). The mean age was 41.2 (SD: 7.4) and 47.3 (SD: 7.5) at first and last diagnosis. Partner notification details were available for 111 of the 139 diagnoses. Overall, 838 contacts were reported, of which 79% were deemed notifiable, 53% notified and 23% reported to have been tested and/or treated. Mean number of sexual contacts per diagnosis was 7.6 (median= 5, range=1-50). SNA identified that over the ten years, 10 and 4 members of this core group were linked directly or indirectly through contacts.

Conclusion: Individuals with multiple syphilis reinfections were virtually all co-infected with HIV and almost half had sexual linkages at some point over 10 years. Routine syphilis testing among HIV patients and high-risk behaviours may account for the multiple syphilis diagnoses. Strategies to protect against syphilis infection, like daily prophylaxis, may benefit individuals in this core group.

EPHP4.05

HIV a Risk factor for Reinfections of Infectious Syphilis among Gay, Bisexual, and Other Men Who Have Sex With Men (MSM) in British Columbia (BC), 2005-2014

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Background: The rate of syphilis has increased in BC, from 6.8 to 11.9 per 100,000 from 2005 to 2014, with MSM disproportionately affected. Syphilis infection risk among MSM is not homogeneous, with small subpopulations most at risk. We sought to characterize and identify early markers for risk of syphilis reinfection among MSM in BC.

Methods: All infectious syphilis diagnoses among MSM from 1/1/2005 to 12/31/2014 were identified through the provincial STI surveillance system. Cases were categorized based on the number of infections (i.e. 1, 2, 3 and ≥4). Bivariate analyses were completed using ANOVA and ordinal regression tests to examine differences by age, ethnicity, HIV status, stage of infection, lifetime history of STI, STI co-infection at the time of diagnosis, and self-reported number of partners during the infectivity period (3-12 months, depending on the infection stage). Variables with $p<0.25$ in the bivariate analysis were assessed in a multivariate model. Characteristics at earliest syphilis diagnosis during the study timeframe were analyzed.

Results: Between 2005-2014, there were 2348 syphilis diagnoses among 1830 MSM: 366 (20%) had two or more infection; 266 (73%) had two, 69 (19%) had three, and 30 (8%) had four or more. An increasing number of syphilis reinfections was positively associated with Caucasian ethnicity, number of self-reported partners, HIV-positivity and a history of gonorrhea, with $p\leq0.05$. In the multivariable model, HIV positivity (aOR:3.8; 95%CI:2.8-5.2,) and self-reported number of partners (aOR: 1.9; 95%CI:1.4-2.7 for 3-5 partners, and aOR:2.5; 95%CI:1.8-3.5 for 6+ partners, both compared to 1-2 partners) remained significantly associated with increasing diagnoses. Addition of stage of infection to the model did not alter the results.

Conclusion: Identification of early markers for syphilis reinfection can help inform targeted prevention strategies. Given our findings, strategies that address the common drivers of syphilis and HIV infection are needed.

EPHP4.06

The Hepatitis C Cascade of Care in a Women-Centered HIV Clinic in Canada

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Background: Worldwide, 5 million people are co-infected with human immunodeficiency virus (HIV) and hepatitis C virus (HCV) however, few data are available to assess the continuum of care from diagnosis, linkage, engagement and treatment for co-infected women. In this descriptive analysis, we assess the HCV cascade of care for patients in a predominantly women's HIV clinic.

Methods: The Oak Tree Clinic (OTC) is a multidisciplinary HIV clinic in Vancouver, Canada. Data for all HIV positive patients ≥18 years old followed in the OTC was retrieved. We describe the characteristics of the cohort focusing on HCV co-infected patients.

Results: A total of 694 patients were included of whom 565 (81%) were female. Mean age was 43 years (IQR 36-50), median CD4 count 557 cells/μL (IQR 350-720) and 526 (76%) patients had an undetectable HIV viral load. HCV antibody (Ab) status was known in 665 (96%) and 261 (38%) were Ab+. Of 261 HCV Ab+ patients, 58 (22%) spontaneously cleared, 33 (13%) were treated with a sustained virologic response, and 13 (5%) had an unknown method of RNA clearance. HCV RNA status was unknown in 8 (3%) patients.

Of 149 HCV RNA+ patients, 145 (97%) had liver fibrosis staging by aspartate aminotransferase-to-platelet ratio index (APRI) and Fibrosis-4 (Fib4) scores, of whom 26 (17%) had severe fibrosis. Currently, 28 (19%) have been referred for HCV therapy, and 4 (2.7%) are on treatment, yet 59 (40%) patients qualify for HCV therapy based on local guidelines.

Conclusion: In this predominantly female population co-infected with HIV and HCV, 17% had evidence of significant fibrosis despite their relatively young age and 40% would qualify for HCV treatment. Despite this, few patients with active HCV infection were on HCV therapy. Enhanced efforts and gender responsive services may be helpful in optimizing access to treatment for HIV/HCV co-infected women.

EPHP4.07

Epidemiology of Spine Infection in Patients with History of IV Drug Use and HIV Infection. Possibility of the Secondary Prevention

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Background: Spine infection is one of the most challenging and multi-disciplinary health conditions for clinicians to manage. Risk factors for this conditionis include IV drug use and HIV infection. An increase in these risk factors has coincided with increased rates of spinal infection in Saskatoon, Saskatcheawan. However, the exact incidence and the clinical significance of spine infection associated with high risk behavior is poorly understood.

Method: A retrospective chart review was completed obtaining information from adult patients with discitis, osteomyelitis, or epidural abscess admitted to the Royal University Hospital, University of Saskatchewan for the last nine years.

Results: This study included 176 patients. The mean age was 54-years-old. 41% had discitis, 69% had osteomyelitis and 45% had an epidural abscess. Overall mortality was 3% and 16% of patients ended up with severe disability. 40% of patients were intravenous drug users, 45% were hepatitis C positive and 12% were HIV positive. The cases of spine infection has been increasing. For the initial six years of our study we experienced 92 patients. We experienced 84 cases over the past three years. This coincides with increasing number of HIV infections in Saskatchewan. Geographical analysis was performed for the city of Saskatoon. High incidence area within the city of was clearly identified.

Discussion and Conclusion: In our study population with spine infection we clearly identified the high risk group of patients. High incidence of IV drug use, Hepatitis C infection, and HIV has an important implication in terms of what measures would assist in prevention of this condition. Secondary prevention or early identification of patients may reduce the number of patients who require lengthy admission, surgical intervention, and long term care for severe disability.

EPHP4.08

A history of HIV and syphilis co-infection in Winnipeg, Manitoba

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Background: A disproportionate burden of syphilis cases is borne by men who have sex with men (MSM) in Winnipeg, Manitoba. Substantial overlap exists between HIV and syphilis infections. The aim of the study was to describe HIV co-infection with incident syphilis over time.

Methods: Data were extracted from public health surveillance databases. HIV co-infection was compared between two time periods: 2004-2011 and 2012-2015, reflecting two distinct outbreaks of syphilis. Generalized linear models compared HIV co-infection over time, and examined the determinants of HIV co-infection; adjusted prevalence ratios (APR) and 95% confidence intervals (95%CI) were produced. Using the Gini coefficient, inequality in geographic distribution of HIV-positive syphilis men was compared over time.

Results: Between 2004-2015, 375 cases of infectious syphilis were reported. HIV co-infection was similar across both time periods (25.2% vs. 26%, p=.862). Mean age at syphilis diagnosis among HIV-positive men was 38.2 years (interquartile range: 33-45), with no statistically significant differences in age, sexual identity and staging of syphilis by time period. In adjusted models, the decrease in HIV prevalence remained non-significant (APR: 1.04, 95%CI: 0.8-1.4, p=0.792). Among HIV-co-infected men, the use of internet-based social media increased (APR: 2.2, 95%CI: 1.2-4.0) in Period 2. As measured by the Gini coefficient, geographic concentration of HIV-co-infected men decreased between Period 1 (0.69, 95%CI: 0.6-0.8) and Period 2 (0.59, 95%CI: 0.4-0.7).

Conclusions: Between 2004 and 2015 the proportion of HIV co-infected men has remained similar across time in Winnipeg. The increasing geographic dispersion of HIV-co-infected men underscores challenges for public health intervention.

Age-standardized Rate of Male Infectious Syphilis Rates and HIV Co-infection, Winnipeg Health Region (2004-2015) (N=281)

Year	Rate (per 100,000)	HIV Positive (%)
2004	7.5	20.0
2005	13.3	34.1
2006	5.7	36.8
2007	7.7	15.4
2008	2.4	37.5
2009	1.2	25.0
2010	1.8	33.3
2011	2.6	44.4
2012	3.7	23.5
2013	9.8	34.3
2014	22.6	24.4
2015	20.2	24.4

EPHP4.09

Is the Face of Hepatitis C Changing in Montreal?

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Background: While HCV sexual-transmission (s-HCV) was long considered a low risk, this micro-phenomenon has

been emerging in the last few years. We seek to assess the change in the epidemiological portrait of HCV in Montreal.

Methods: All HCV-infected patients attending Clinique médicale l'Actuel were assessed retrospectively. Information on demographics, risk factors and HIV were collected from an electronic database. Analyses were done by Chi2 and ANOVA.

Results: 1628 patients were included (±50 new HCV/y). Risk factors for HCV-transmission are injection drug use (IDU) (75%), s-HCV (7%) and originating from endemic region (4%). Since 2007 we observe a steady decline in the overall incidence of HCV-infections. When comparing modes of transmission by sexual orientation, we noted growing s-HCV in MSM: for the period of 2000-2007 IDU and s-HCV transmissions were stable, but since 2007 s-HCV (30% to 74%) has increased greatly; also 72% of HCV-infections were diagnosed in HIV-coinfected patients (vs. 57% ≤2007;p=0.047). In heterosexuals HIV-coinfection was less prevalent (8% coinfection >2007 vs. 20% ≤2007;p<0.001). We suspect the increase in crystal meth use is a possible contributing factor to this trend as its use has doubled since 2007 among our catchment population (10% in 2007 to 19% in 2014). Another is the decrease of protected sexual behaviour and growing STD epidemic, as the number of HCV diagnosed with concomitant STDs (syphilis/HIV/gonorrhea/chlamydia) has been on the rise since 2009 (16% to 71% in 2012;p=0.02). The only HCV-genotype that was differently distributed among pre 2007 and post 2007 was genotype-2 (5% ≤2007 vs 12% >2007;p=0.001).

Conclusion: Current trends in the epidemiology of HCV in Montreal include an apparent increase in sexual transmission, particularly in MSM population. Injection drug use no longer seems to be the prominent risk factor for HCV infection among Montreal MSM. Not all sexually transmitted HCV occur in HIV-coinfected patients.

Epidemiology and Surveillance of HIV/AIDS
Épidémiologie et surveillance of du VIH/sida

EPHP5.01

I-Track: Enhanced surveillance of HIV and hepatitis C risk behaviours among people who inject drugs in Canada, 2002 to 2012

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Background: I-Track, an enhanced surveillance system that monitors HIV and hepatitis C risk behaviours among people who inject drugs, was conducted in sentinel sites across Canada in 2002-2003 (Pilot), 2003-2005 (Phase 1-P1), 2005-2008 (Phase 2-P2), and 2010-2012 (Phase 3-P3).

Methods: Information regarding demographics, drug use, injecting and sexual risk behaviours, and HIV and hepatitis C testing patterns were collected in confidential, anonymous face-to-face interviews in four sites in the Pilot, seven sites in P1, ten sites in P2 and eleven sites in P3. A biological sample was collected for HIV antibody testing. Selected descriptive statistics were compared across time.

Results: A total of 793, 2986, 2982 and 2687 participants were interviewed in the Pilot, P1, P2, and P3 surveys, respectively. Demographic characteristics varied slightly across phases: the majority of participants were male (64.8%-69.8%), the average age ranged from 35.0 to 39.4 years and the proportion that self-identified as Aboriginal ranged from 26.5% to 43.6%. The drug most often injected was cocaine (29.4%-54.2%) and recent increases in opiate use, including oxycodone, were noted. Less than a quarter of participants borrowed used needles (15.5%-23.6%), mostly from sex partners (34.8%-51.4%) or friends/family (34.1%-43.8%). The majority reported ever testing for HIV (90.0%-92.9%) and 77.6%-84.1% tested within the previous 2 years. Overall HIV prevalence ranged from 7.0%-14.9%, with a decline observed from P1 to P3. Overall, 20.3%-24.1% of HIV positive participants were unaware of their HIV positive status and 85.9%-93.3% reported being under the care of a doctor for their HIV infection.

Conclusions: This comparison across I-Track phases presents a national profile of risk behaviours over a 10 year period. The observed decreases in HIV prevalence since P1 echoes the declining trends observed nationally for HIV incidence and diagnoses attributed to injection drug use exposure.

EPHP5.02

Factors Associated with Incidence of Type 2 Diabetes among HIV-Positive and HIV-Negative British Columbians

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Background: This study examines the incidence and correlates of type 2 diabetes diagnosis (T2DM) among HIV-positive and HIV-negative individuals in British Columbia (BC).

Methods: Using data from the Comparison of Outcomes and Service Utilization Trends (COAST) study, incidence of and factors associated with type T2DM were calculated from 1996 to 2013. HIV-negative and HIV-positive individuals who have ever been on HAART were included. Cases of T2DM were identified through physician billing and hospital administrative data using International Classification of Disease 9/10 codes. Logistic regression was conducted to model T2DM, with AIC-based backward elimination.

Results: Overall, 9,432 HIV-positive and 514,619 HIV-negative individuals were included, of which, respectively, 17.3% and 49.7% were female, 33.8% and 1.9% used

injection drugs (IDU), 13.4% and 0.3% were Hepatitis C virus (HCV) seropositive, with median age of 37 (1st-3rd quartile (Q1-Q3): 31-45) and 35 (Q1-Q3: 23-49). Among the HIV-positive and HIV-negative populations, respectively, we identified 444 (4.7%) and 25,624 (5.0%) prevalent and 320 (4.1%) and 22,293 (4.9%) incident cases of T2DM, with incidence rates of 3.9 (95% Confidence Interval (CI): 3.5-4.4) and 4.0 (CI: 3.9-4.0) per 1,000 individuals per year.

Results from multivariable analysis are presented in table 1. Adjusting for socio-demographic and clinical variables, HIV-positive status was significantly associated with T2DM (odds ratio: 1.19, CI: 1.05-1.35).

Conclusion: Results indicate there are significant differences in factors associated with T2DM between HIV-positive and HIV-negative populations in BC. Differences were found for sex, health authority of residence, IDU, post-secondary education level and prior non-alcoholic fatty liver disease diagnosis.

Table 1: Multivariable Analysis: Factors Associated with Type 2 Diabetes Diagnosis

Variable	Whole sample	HIV-positive
HIV status		
HIV-negative	1.00 (Ref)	
HIV-positive	1.19 (1.05-1.35)	
Sex		
Female	1.00 (Ref)	1.00 (Ref)
Male	1.38 (1.34-1.42)	0.88 (0.62-1.24)
Health authority		
Interior Health	1.00 (Ref)	1.00 (Ref)
Fraser Health	1.33 (1.27-1.40)	1.25 (0.73-2.13)
Vancouver Costal Health	1.18 (1.12-1.24)	0.92 (0.55-1.54)
Island Health	1.07 (1.02-1.13)	1.22 (0.68-2.18)
Northern Health	1.64 (1.54-1.74)	0.54 (0.18-1.64)
Unknown	0.32 (0.21-0.48)	n/a
Hepatitis C seropositivity		
No	1.00 (Ref)	1.00 (Ref)
Yes	1.76 (1.50-2.07)	2.51 (1.81-3.49)
Injection drug use		
No	1.00 (Ref)	1.00 (Ref)
Yes	1.55 (1.42-1.69)	0.77 (0.56-1.05)
Ischemic heart disease diagnosis		
No	1.00 (Ref	1.00 (Ref
Yes	1.50 (1.45-1.55)	1.4 (1.01-1.93)
Nonalcoholic fatty liver disease diagnosis		
No	1.00 (Ref)	1.00 (Ref)
Yes	2.54 (1.92-3.35)	1.73 (0.51-5.87)
Hypertension diagnosis		
No	1.00 (Ref)	1.00 (Ref)
Yes	2.01 (1.95-2.08)	2.04 (1.58-2.65)
Post secondary education (census tract)		
<50%	1.00 (Ref)	1.00 (Ref)
≥50%	0.72 (0.69-0.74)	0.88 (0.65-1.19)
Baseline age (by 10 years)	1.59 (1.57-1.61)	1.88 (1.66-2.14)
Ethnicity		
Caucasian		1.00 (Ref)
Indigenous		1.19 (0.8-1.76)
Other/mixed		1.95 (1.28-2.97)
Unknown		1.04 (0.75-1.45)
ART interruption of 3 months		
No		1.00 (Ref)
Yes		0.75 (0.56-0.99)
Unknown		0.55 (0.25-1.22)
HAART regimen at diabetes diagnosis		
PI based		1.00 (Ref)
NNRTI based		0.52 (0.37-0.71)
Other		0.86 (0.65-1.14)
HAART adherence		
<90%		1.00 (Ref)
>=90%		1.53 (1.14-2.06)
Missing		2.09 (1.3-3.36)
CD4 cell count at time of diabetes diagnosis (cells/µL)		
≥500		1.00 (Ref)
350-499		1.07 (0.76-1.51)
200-349		2.01 (1.46-2.78)
0-199		1.35 (0.91-2)
Missing		25.12 (4.6-137.21)
Viral load at diabetes (copies/mL)		
≤35		1.00 (Ref)
36-100		2.87 (2.07-3.97
101-10,000		3.04 (2.06-4.49)
> 10,000		4.07 (2.71-6.1)
Results are odds ratio (95% confidence interval)		

EPHP5.03

Factors Associated with Mood Disorder Diagnosis Among HIV-Positive and HIV-Negative Individuals in British Columbia

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Background: This study describes differences in prevalence, incidence and factors associated with mood disorder (MD) among HIV-positive and HIV-negative populations in British Columbia (BC).

Methods: Using the Comparison of Outcomes And Service Utilization Trends (COAST) cohort, a population-based retrospective study examining health outcomes and service use of HIV-positive and a random 10% sample of individuals in BC, prevalence and incidence of MD were identified and calculated from 1996 to 2013, using physician billing and hospital-based administrative data and International Classification of Disease 9/10 codes. Logistic regression was conducted to model the association be-

tween MD diagnosis and socio-demographic and clinical characteristics, with AIC-based backward elimination.

Results: Overall, 514,619 HIV-negative and 9,432 HIV-positive individuals were included. HIV-negative and HIV-positive individuals were, sequentially, 49.7% and 17.3% female, 0.3% and 13.4% infected with Hepatitis C virus (HCV), with median age 35 (Q1-Q3: 23-49) and 37 (Q1-Q3: 31-45). We identified 86,022 (16.7%) and 3,870 (41.0%) prevalent cases and 60,834 (12.4%) and 1,656 (24.6%) incident cases of MD among the HIV-negative and HIV-positive populations, respectively.

In multivariable analysis, HIV-positive individuals were significantly more likely to be diagnosed with MD (adjusted odds ratio (aOR): 1.79 (95% CI=1.67-1.92). HCV seropositivity, injection drug use, prior anxiety diagnosis, and prior dysthymia diagnosis were significantly associated with MD diagnosis. Full multivariable results are shown in table 1.

Conclusions: Our results indicate that MD diagnosis is more prevalent in the HIV-positive compared to the HIV-negative population, and is associated with prior diagnoses of other mental health conditions and history of substance use.

Table 1: Multivariable analysis of factors associated with mood disorder diagnosis among HIV-positive and HIV-negative individuals in British Columbia

Variable	Whole sample aOR(95%CI)	HIV-positive aOR(95%CI)
HIV status		
HIV-negative	1.00 (Ref)	
HIV-positive	1.76 (1.64-1.89)	
Sex		
Female	1.00 (Ref	1.00 (Ref)
Male	0.54 (0.53-0.55)	1.02 (0.86-1.21)
Health Authority		
Interior Health	1.00 (Ref)	1.00 (Ref)
Fraser Health	0.82 (0.80-0.85)	0.57 (0.43-0.76)
Vancouver Costal Health	0.74 (0.72-0.76)	0.64 (0.49-0.83)
Island Health	1.03 (1.00-1.06)	0.84 (0.62-1.13)
Northern Health	0.86 (0.83-0.90)	0.66 (0.42-1.04)
Unknown	0.65 (0.58-0.73)	0.18 (0.02-1.42)
Hepatitis C seropositivity		
No	1.00 (Ref)	1.00 (Ref)
Yes	1.18 (1.06-1.32)	1.39 (1.16-1.67)
Injection drug use		
No	1.00 (Ref)	1.00 (Ref)
Ye	4.45 (4.22-4.68)	2.89 (2.36-3.54)
Substance use disorder		
No	1.00 (Ref)	1.00 (Ref)
Yes	1.42 (1.37-1.47)	0.75 (0.62-0.91)
Anxiety diagnosis		
No	1.00 (Ref)	1.00 (Ref)
Yes	2.2 (2.1-2.29)	1.56 (1.26-1.94)
Dysthymia diagnosis		
No	1.00 (Ref)	1.00 (Ref)
Yes	5.47 (4.87-6.14)	2.20 (1.62-2.98)
Somatic symptom disorder		
No	1.00 (Ref)	1.00 (Ref)
Yes	1.11 (1.04-1.18)	1.13 (0.75-1.69)
Post secondary education		
<50%	1.00 (Ref)	1.00 (Ref)
≥50%	0.94 (0.92-0.96)	1.63 (1.39-1.93)
Employment		
<60%	1.00 (Ref)	1.00 (Ref)
≥60%	1.15 (1.12-1.17)	1.13 (0.97-1.32)
Baseline age (by 10 years)		0.88 (0.81-0.96)
HAART regimen at mood disorder		
PI based		1.00 (Ref)
NNRTI based		1.46 (1.23-1.73)
Other		1.15 (0.96-1.38)
Earliest HIV record year		
Prior to 1999		1.00 (Ref)
1999-2003		1.63 (1.32-2.01)
2004-2007		2.86 (2.16-3.78)
2008-2013		1.36 (0.84-2.21)
HAART adherence		
<90%		1.00 (Ref)
≥90%		1.29 (1.09-1.52)
Missing		1.82 (1.29-2.56)
CD4 cell count at time of mood disorder diagnosis		
≥500		1.00 (Ref)
350-499		1.14 (0.94-1.39)
200-349		1.24 (1.01-1.52)
0-199		0.85 (0.68-1.07)
Missing		19.78 (5.75-68.00)
Viral load at mood disorder		
≤35		1.00 (Ref)
36-100		14.02 (11.54-17.02)
101-10,000		13.74 (10.98-17.21)
> 10,000		18.36 (14.56-23.16)
Missing		2.78 (0.59-13.04)

EPHP5.04

HIV Incidence Rate and Predictors Among Gay and other Men Who Have Sex With Men (MSM) in Vancouver: Additional Benefit of an Administrative Health Data Linkage

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Background: We calculated HIV incidence rates and identified seroconversion predictors in a cohort study of MSM in Vancouver, British Columbia (BC).

Methods: Sexually-active MSM aged ≥16 years were enrolled starting 02/2012 in a longitudinal cohort study recruited using respondent-driven sampling. Study visits occurred every six months and included a computer-assisted self-interview on demographics, sex and substance use, and a nurse-administered sexual health check-up with point-of-care HIV testing. Participants consented to data linkages with the BC Centre for Excellence in HIV/AIDS's databases containing all provincial HIV viral load and treatment data. We calculated HIV incidence rates overall, by age-group, and using the HIV Incidence Risk Index for MSM (HIRI-MSM, range 0-45). We examined factors associated with HIV seroconversion using Poisson regression (adjusted for follow-up time).

Results: As of August 31, 2015, 497 MSM who tested HIV-negative at enrolment contributed a mean follow-up time of 2.23 years, were 82.7% gay-identified, 74.5% White, and 40.9% were aged ≤30. HIV incidence rates are shown in the table below. Of 12 seroconversions recorded, 6 occurred during study follow-up and an additional 6 were identified through the data linkage. HIV seroconversion was significantly associated with crystal methamphetamine- and gamma-hydroxybutyrate-use during sex, group sex event participation, more sexual partners, less condom use, previous STI diagnosis, and being born outside Canada ($p<0.05$ for all).

Conclusions: Data linkage identified twice as many seroconversions than observational cohort follow-up alone. MSM who seroconverted demonstrated several syndemic factors, which may help target combination HIV prevention towards MSM most likely to acquire HIV.

	Number of Seroconversions	HIV Incidence Rate per 100 person-years
(95% Confidence Interval)		
Overall (with data linkage)	12	1.08 (0.62-1.90)
Only Cohort Follow-Up (without data linkage)	6	0.79 (0.35-1.76)
Aged ≤30 (with data linkage)	8	1.80 (0.90-3.62)
Aged >30 (with data linkage)	4	0.60 (0.23-1.59)
HIRI-MSM ≥10 (with data linkage)	12	2.04 (1.16-3.59)
HIRI-MSM ≥25 (with data linkage)	7	7.04 (3.34-14.85)

EPHP5.05

Clinical and socio-demographic characteristics and early ART initiation during Primary HIV Infection

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Introduction: Early diagnosis and prompt ART initiation reduce disease progression, prevent secondary transmission and represent the only undisputed strategy to curtail HIV reservoir size. Primary HIV infection (PHI) provides a window of opportunity for early intervention and here we determine the clinical and socio-demographic factors associated with treatment initiation.

Methods: A total of 336 adult HIV-1-infected individuals participating in the Montreal Primary HIV Infection Study (1996-2014) with an estimated date of HIV acquisition of less than 180 days were studied. Clinical and socio-demographic characteristics of PHI study participants initiating (n=219) or not (n=117) ART within the first six months were compared. Patients were recruited in three community clinics (165) and in five hospital centres (171) throughout Montreal.

Results: Majority of the PHI participants were male (95.7%), MSM (78.7%), Caucasian (81.1%), single (45.8%) with an average age of 36±10 years. They presented with a median CD4 T-cell count of 510 cells/uL, CD8 T-cell count of 810 cells/uL and a viral load of 4.6 log-copies/mL. Early ART initiation was observed in 65.4% of PHI participants. The proportion of patients who initiate ART during the first six months was about 63%, 50%, 71% and 91% for every five year interval. Gender, ethnicity, usage of IV drugs and number of sexual partners in the last three months, being followed at community medical clinics or hospitals was not associated with early ART initiation. In contrast, lower income and being unemployed was associated with delayed ART initiation ($p=0.021$) and was consistent over time.

Conclusions: Lower socio-economic status independently delays ART initiation in recently diagnosed individuals. Advancement in ART and results from clinical trials supporting early ART initiation are key drivers for the very early treatment initiation. Such information will be relevant to scale up strategies aiming at a functional cure.

EPHP5.06

Prevalence and correlates of reporting antiretroviral therapy is difficult to take among HIV-positive illicit drug users in Vancouver, Canada

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Background: People living with HIV/AIDS who use illicit drugs continue to experience high rates of suboptimal treatment outcomes from antiretroviral therapy (ART). Although previous studies have identified important barriers to ART adherence, such as ongoing drug use, the effect of patient-level factors have not been fully evaluated. Thus, we sought to investigate the prevalence and correlates of reporting ART was difficult to take among a cohort of illicit drug users in Vancouver, Canada.

Methods: We accessed data from the AIDS Care Cohort to evaluate Exposure to Survival Services (ACCESS), an ongoing prospective cohort of HIV-positive illicit drug users linked to comprehensive HIV/AIDS clinical monitoring records. We used generalized linear mixed-effects modeling to identify factors longitudinally associated with self-reporting ART is difficult to take.

Results: Between December 2005 and May 2014, 746 ART-exposed illicit drug users were recruited and contributed at least one study interview. At baseline, 209 (28%) reported they found ART hard to take. Over the study period, reporting ART was hard to take was positively associated with factors including reporting barriers to healthcare (AOR = 1.64, 95% CI: 1.34–2.01); and a greater daily pill count (AOR = 1.12 per pill, 95% CI: 1.08–1.17). Reporting ART was hard to take was negatively associated with being satisfied with their HIV physician (AOR = 0.76, 95% CI: 0.58–1.00); and exhibiting a non-detectable VL (AOR = 0.62, 95% CI: 0.52–0.75).

Conclusion: In this community-recruited cohort of ART-exposed illicit drug users, a substantial proportion reported they found treatment hard to take, which was clearly linked to a lower likelihood of experiencing optimal virologic outcomes. Our findings reveal a number of opportunities to improve HIV/AIDS treatment experiences and outcomes for people who use illicit drugs, including the use of treatment regimens with lower pill burdens.

EPHP5.07

Incidence and Survival of Non-Small-Cell Lung Cancer Among HIV Positive and HIV Negative Individuals in British Columbia, Canada

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Background: The objective of this study is to determine the incidence and survival of non-small-cell lung cancer (NSCLC) among HIV+ and HIV- individuals in BC, Canada.

Methods: This study uses data from the Comparison of Outcomes and Service Utilization Trends (COAST) over the period from 1998-2011. HIV+ individuals were identified using a case-finding algorithm, while HIV- individuals were identified from a 10% sample of the BC population. We identified NSCLC cases using International Classification of Disease for Oncology, 3rd ed. codes. Prevalent cases of NSCLC from 1998-2000 were excluded from analysis. Survival analysis comparing HIV+ to HIV- was done with Kaplan-Meier and Cox models, controlling for age, gender, and comorbidities.

Results: We identified 59 HIV+ and 2171 HIV- individuals with NSCLC. Incidence of NSCLC from 2009-2011 was higher among HIV+ (0.73 [0.44-1.126]/1000 person-years [PY]) than HIV- (0.46 [0.41-0.49]/1000PY). Median survival from NSCLC diagnosis was 4 months for HIV+ and 10 months for HIV-. Overall survival for HIV+ individuals was significantly shorter than HIV- (p = <0.01).

Table 1 shows the results of the univariate and multivariable analysis. Although not significant in the HIV+ population, male gender was significantly associated with mortality among HIV- individuals. In multivariable analysis, HIV+ individuals were 33% more likely to die than HIV- individuals (adjusted hazard ratio [AHR]:1.33 95% CI: 0.99-1.8).

Conclusion: Our results indicate that NSCLC prognosis among HIV+ individuals is associated with gender and presence comorbidities, such as hepatitis B. Survival time from NSCLC diagnosis to death was significantly shorter for the HIV+ population.

Table 1: Univariate and multivariable analysis of factors associated with mortality among HIV+ and HIV- individuals diagnosed with NSCLC in British Columbia

Variable	HIV+ hazard ratio (95% CI)	HIV- hazard ratio (95% CI)	Whole sample adjusted hazard ratio (95% CI)
HIV-	--	--	1.00 (REF)
HIV+	--	--	1.33 (0.99-1.80)
Age			
[15-44]	1.00 (REF)	1.00 (REF)	1.00 (REF)
[45-59]	0.91 (0.27-3.04)	1.25 (0.73-2.15)	1.16 (0.71-1.89)
[60-69]	0.74 (0.21-2.62)	1.28 (0.75-2.19)	1.15 (0.71-1.87)
[70-79]	0.78 (0.18-3.31)	1.29 (0.76-2.19)	1.15 (0.71-1.87)
[80+]	0.37 (0.06-2.25)	1.70 (1-2.9)	1.50 (0.92-2.44)
Year of cancer diagnosis			
[2000-2002]	1.00 (REF)	1.00 (REF)	--
[2003-2005]	1.58 (0.7-3.57)	1.00 (0.87-1.14)	--
[2006-2008]	1.17 (0.53-2.6)	0.91 (0.79-1.04)	--
[2009-2011]	1.09 (0.49-2.41)	0.61 (0.52-0.7)	--

Sex			
Female	1.00 (REF)	1.00 (REF)	1.00 (REF)
Male	0.44 (0.19-1.06)	1.28 (1.16-1.41)	1.27 (1.15-1.4)
CVD			
No	1.00 (REF)	1.00 (REF)	--
Yes	1.06 (0.56-2)	1.00 (0.9-1.1)	--
Liver			
No	1.00 (REF)	1.00 (REF)	--
Yes	1.55 (0.89-2.69)	1.07 (0.82-1.4)	--
Renal			
No	1.00 (REF)	1.00 (REF)	1.00 (REF)
Yes	0.67 (0.32-1.38)	1.24 (1.02-1.51)	1.12 (0.93-1.36)
Hep B			
No	1.00 (REF)	1.00 (REF)	1.00 (REF)
Yes	3.61 (1.92-6.78)	1.09 (0.61-1.98)	1.86 (1.26-2.74)
Hep C			
No	1.00 (REF)	1.00 (REF)	--
Yes	1.44 (0.52-4.03)	0.52 (0.17-1.62)	--
IDU			
No	1.00 (REF)	--	--
Yes	1.69 (0.94-3.05)	--	--
Unknown	0.86 (0.35-2.14)	--	--
CD4 count			
0-200	1.00 (REF)	--	--
201+	0.58 (0.33-1.03)	--	--
Unknown	0.60 (0.08-4.47)	--	--
Viral load			
0-100000	1.00 (REF)	--	--
100001+	0.62 (0.3-1.31)	--	--
Unknown	0.85 (0.44-1.65)	--	--
Treatment Interruption			
No	1.00 (REF)	--	--
Yes	1.16 (0.64-2.08)	--	--
Cancer Stage			
I	1.00 (REF)	1.00 (REF)	--
II	0.81 (0.05-12.93)	4.55 (1.75-11.83)	--
III	0.00 (0-Inf)	5.98 (2.5-14.29)	--
IV	8.32 (0.96-71.8)	14.28 (6.29-32.42)	--
Unknown	2.80 (0.38-20.43)	11.89 (5.33-26.51)	--

Evaluations of Public Health Programs and Interventions
Évaluation des programmes et des interventions en santé publique

EPHP6.01

What Sets it Apart: Client Experiences at the Dr. Peter Centre

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Background: The Dr. Peter Centre (DPC) is an integrative health care facility for people living with HIV (PLHIV) who have complex care needs. The DPC services are designed to engage individuals in their health care. There is limited evidence of the impact of this approach on clients' perception of the DPC. The present analysis aims to gauge DPC client attitudes.

Methods: A quantitative baseline survey covering eight domains was administered to individuals who have been DPC clients since 27 February 2011. We used data derived from descriptive statistics and survey frequency counts to create word clouds. Word clouds were created by tabulating text response frequencies for select questions using Wordle (www.wordle.net); words were only included if they had a response frequency of n ≥2.

Results: Between February 2014 and April 2015, 121 participants completed the quantitative baseline survey. Overall, 99 (82%) were male, 43 (36%) were of Indigenous ancestry, 53 (44%) identified as heterosexual, 63 (52%) had ever been incarcerated, and 100 (83%) had ever been homeless. The median age was 46 (Q1-Q3: 39-52) years. Based on survey responses, 90% of participants always felt respected by staff, 96% felt welcomed by staff always or most of the time, 93% felt cared for by DPC staff and 91% felt a sense of belonging always or most of the time. The words most frequently used to describe what sets the DPC apart from other healthcare facilities are: caring, food, and staff.

Conclusions: Results suggest study participants feel positively about the DPC staff and environment. This is an important finding, as clients' perceptions may impact engagement with health care and services. Analyses such as this can help inform how to respond to the needs of PLHIV with complex care issues, and offers a novel approach to presenting findings back to the client community.

EPHP6.02

HIV Researchers Mentoring the Next Generation of Clinician Scientists

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Objectives: The high level of substance use disorders among HIV positive individuals, and the negative impact of substance use on HIV treatment outcomes, warrant innovative educational activities to scale up the use of novel treatments for these dual issues. Although the large evidence-base upon which to base clinical practice keeps growing, most health systems have not invested in combined training of healthcare providers in issues related to HIV/ addiction medicine and research. As such, HIV- and addiction- related care is often lacking, or not based on evidence or best practices. We undertook a qualitative study to assess the experiences of physicians who completed clinician-scientist training in HIV/ addiction medicine within a hospital setting.

Methods: We interviewed physicians from the St. Paul's Hospital Goldcorp Addiction Medicine Fellowship and learners from the hospital's academic Addiction Medicine Consult Team in Vancouver, Canada (N=26). They included psychiatrists, internal medicine and family medicine physicians, faculty, mentors, medical students and residents. All received both addiction medicine and research training. Drawing on Kirkpatrick's model of evaluating training programmes, we analysed the interviews thematically using qualitative data analysis software (Nvivo 10).

Results: We identified five themes relating to learning experience that were influential: (i) attitude, (ii) knowledge, (iii) skill, (iv) behaviour and (v) patient outcome. The presence of a supportive learning environment, flexibility in time lines, highly structured rotations, and clear guidance regarding development of research products facilitated clinician-scientist training. Competing priorities, to include clinical and family responsibilities, hindered training.

Conclusion: Combined training in addiction medicine and research is feasible and acceptable for current doctors and physicians in training. However, there are important barriers to overcome and improved understanding of the experience of physicians in the clinician-scientist track is required to improve curricula, research productivity, and health outcomes of people living with HIV/AIDS.

EPHP6.03

Nutritional status, Symptoms of depression and anxiety among patients living with HIV on Highly Active Anti Retroviral Therapy in Malaysia

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The prevalence of depression in HIV patients has been increasing but this has not been well documented particularly the depression incidence among under-nourished HIV patients. The present study aimed to evaluate the association between nutritional status and symptoms of depression and anxiety among people living with HIV (PLHIV) receiving highly active antiretroviral therapy (HAART). The cross-sectional study was conducted in an outpatient infectious disease (ID) clinic in Malaysia. A total of 170 HIV patients were evaluated for socio-demographic characteristics and nutritional status using Scored Patient-Generated Subjective Global assessment (PG-SGA), Body Mass index (BMI), Mid Upper Arm Circumferences (MUAC) and serum haemoglobin (Hb). The patients were then subjected to self-administrated questionnaire containing the Hospital Anxiety and Depression Scale (HADS). HADS Scores showed a depression rate of 52.4% among the respondents while based on PG-SGA, 87 subjects indicated the symptoms of under-nutrition (Stage B and Stage C). Evaluation of socio-demographic and clinical characteristics among well-nourished and under-nourished subjects revealed that there were significant relationship between malnutrition and smoking ($\chi^2 = 9.09$, $P < 0.01$), recreational drug use ($p < 0.05$), BMI ($P < 0.01$) as well as depression ($P < 0.05$).Multiple Linear regression analysis showed a dependence of nutritional status using PG-SGA by smoking ($p=0.03$), BMI ($p=0.01$) and HADS ($p=0.04$). Poor nutritional status was associated with symptoms of anxiety and depression in people infected with HIV. Furthermore, the high prevalence of depression suggested the need to monitor the psychological state in PLHIV.

EPHP6.04

Demand for Anonymous HIV Testing (AHT) in British Columbia (BC) for Clients Vulnerable to HIV Infection

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Background: Stigma associated with HIV poses barriers to accessing testing for vulnerable populations in BC. AHT allows individuals to test without identifying information and retrieve results using a numbered code. The objectives of this evaluation presentation were to understand the demand for and uptake of AHT among clients vulnerable to HIV infection.

Methods: We analyzed data collected between January 2013 and September 2015, from 8 clinics and outreach sites offering AHT in BC. Clinic staff offered a confidential paper survey to all AHT clients, which included questions on risk factors and clinic selection. In summer 2015, staff/providers who offer AHT were invited to complete an online survey, which included items on their opinions and experiences with AHT.

Aggregate AHT volumes were collected through an STI electronic medical record system. Serological results were identified in the provincial laboratory information system.

Results: A total of 373 clients opted for AHT of whom 329 (88%) were male (median age=38 years). The positivity rate for AHT was 1.6% (6/373), which is higher than the provincial STI clinic (0.25%).

Of these, 117 clients (31%) completed the survey. Among survey respondents, 66% identified as men who have sex with men and 22% reported drug use with items shared with others (e.g. needle, cooker or pipe). The majority (72%) of surveyed clients came specifically because the clinic offered AHT.

A total of 35 providers/staff completed a survey. Most providers agreed to the statements that AHT was a key reason their clients attended the testing site (n=21, 60%) and that there are benefits to AHT even with other testing options available (n=29, 83%).

Conclusions: AHT in BC was reported to be a valuable service by clients vulnerable to HIV infection and providers alike and yielded a much higher case-detection rate than at other low-threshold STI testing sites.

HIV Prevention for Key Populations
La prévention du VIH dans les populations clés

EPHP7.01

The Cedar Project: Understanding the increased vulnerability to contracting Herpes Simplex Virus 2 among a cohort of young Aboriginal people who use drugs in British Columbia

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Introduction: Outbreak investigations and national surveillance literature demonstrate that Aboriginal people are disproportionately at risk for contracting sexually transmitted infections (STIs). This reality is even more evident among Aboriginal people who use drugs. Ulcerative STIs, such as Herpes Simplex Virus 2 (HSV-2), not only impact quality of life but also play a role in increasing susceptibility to contracting HIV. The factors associated with increased likelihood of HSV-2 positivity among this vulnerable group need to be better understood.

Methods: The Cedar Project is an ongoing prospective study of Aboriginal young people who use drugs and live in Vancouver, Prince George, or Kamloops, BC. This analysis includes data from October 2012 through to June 2013. Laboratory tests were used to establish point estimates of HSV-2 seroprevalence. Questionnaire data were linked to clinical test results to explore risk factors for HSV-2 seropositivity. After identifying potential associations from bivariate data, forced multivariable logistic regression analysis was used to model independent associations with HSV-2 seropositivity, stratified by gender.

Results: Of the 143 women tested, 74% tested positive. HSV-2 positivity was independently associated with having been taken away from biological parents (Adjusted Odds Ratio: 7.52, 95% Confidence Interval: 2.18-18.84); having a mother who attended residential school (AOR: 2.57 [1.28-6.23]), recent heavy alcohol drinking (AOR: 3.56 [1.34-7.89]), and ever having injected drugs (AOR: 2.34 [1.81-2.71]). Marginally significant associations included a history of sexual abuse (AOR: 1.13 [0.97-1.15]), ever having been involved in survival sex work (AOR: 4.91 [0.88-9.88]), and recent crack smoking. (AOR: 1.67 [0.89-5.34]). Among men (n=107), 36% tested positive. HSV-2 positivity was independently associated with ever having been in prison (AOR: 2.50 [1.68-9.20]). Having participated in traditional ceremonies had a protective effect on HSV-2 positivity (AOR: 0.74 [0.58-0.88]).

Conclusion: Sexual health programming that is culturally tailored and gender specific must be coupled with harm reduction programs to intervene in the pathways of risk factors for STI infections that reduce quality of life and increase risk for contracting HIV.

EPHP7.02

HIV Point-of-Care Testing (HIV POCT): Mobilizing for Change at the National Level

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Background: Although HIV point-of-care testing (HIV POCT) was approved for use in Canada in 2005, access to such testing innovation remains variable, particularly in non-urban settings. National leadership is required in order to ensure access to and uptake of HIV testing remain important elements in both HIV prevention and treatment. As it currently stands, HIV POCT is not available in the 4 Atlantic Provinces and is variably accessible in other jurisdictions. Increased opportunities for HIV and STBBI testing may serve an important public health role in encouraging timely access to treatment, care and support for those who test positive.

Methods: A series of face-to-face and teleconference discussions took place between June and December 2015 with members of the National Working Group on HIV POCT, as well as members of regional and provincial networks from government, community, and research. A consensus building approach lead to the development of a series of recommended actions aimed at addressing micro-, meso- and macro-level barriers to improved access and uptake of HIV POCT in Canada.

Results: A total of 10 recommended actions, including increasing awareness, access, training, education, collaboration, improving testing rates, developing innovation in testing approaches, reminding individuals about the importance of testing, the development of national standards and billing codes for POCT where they do not currently exist were incorporated into the final version of the HIV Point-of-Care Testing (POCT) in Canada: Action Plan 2015-2020.

Conclusion: The development of recommended actions for HIV POCT offers opportunities for partners from government, community, research and industry sectors to mobilize for change to address the current gaps in the provision of testing in Canada. In keeping with the Public Health Agency of Canada approach to integration of STBBI, additional national leadership is required to meet these goals.

EPHP7.03

The importance of collaborative knowledge sharing: Enhancing Canada's policy advice mechanisms on HIV and AIDS under an integrated approach to STBBIs

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Background: The Ministerial Advisory Council on the Federal Initiative to address HIV/AIDS (MAC-FI) in Canada was created in 1998 to advise the Minister of Health on aspects of HIV/AIDS that have a national scope. The National Aboriginal Council on HIV/AIDS (NACHA), formed in 1998, provides Aboriginal-focused, unbiased, non-partisan, evidence-informed and strategic expert advice to the Public Health Agency of Canada (Agency) and the First Nations and Inuit Health Branch (FNIHB) of Health Canada on Aboriginal Peoples HIV/AIDS and hepatitis C and related health factors.

Methods: Recently MAC-FI and NACHA began holding joint meetings in an effort to share lessons learned and to develop policy advice for the Minister of Health and the Public Health Agency of Canada on issues of national importance concerning HIV and AIDS, Hepatitis C and related health conditions. Both external advisory bodies now include an ex-officio representative to help ensure continued information sharing of advice generated in monthly working group teleconferences as well as an annual face-to-face to meeting involving all members. Additional external and government experts also attend meetings to share updates and developments with both groups simultaneously.

Results: Based on recent meetings, the collaborative structure has assisted in ensuring key health issues, relevant to both external advisory bodies, have led to improved timeliness for updates and a more robust and intersectional approach to analyzing and informing policy-related decision-making.

Conclusion: As Canada shifts focus toward an integrated approach to STBBIs, joint meetings between MAC-FI and NACHA will provide a more comprehensive approach to advising on policy responses to the evolving Canadian context. We anticipate that this collaborative strategy will provide a useful template for other sectors to benefit from First Nation, Inuit, and Metis ways of knowing.

EPHP7.04

A 4-Year Longitudinal Event-Level Analysis of HIV Risk and Substance Use Among HIV-Negative and HIV-Positive Gay, Bisexual and Other Men Who Have Sex with Men (MSM)

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Background: We examined event-level trends in sexual HIV risk and substance use among Vancouver MSM during Treatment as Prevention scale-up.

Methods: Sexually-active MSM aged ≥16 years were recruited beginning 02/2012 into a prospective cohort study using respondent-driven sampling. Study visits occurred every six months until 08/2015 and included event-level reports on participants' last sexual episode with their five most recent partners. Generalized estimating equations were used to construct hierarchical logistic regression models (within participant, within visit). Stratified by HIV status, we tested event-level temporal trends and interactions for the effect of substance-use over time on sexual HIV risk (condomless anal sex with a discordant or unknown status partner).

Results: With a median follow-up of 1.50 years, 550 HIV-negative MSM reported 5935 sexual events (17.1% included sexual risk) and 218 HIV-positive MSM reported 2196 events (25.3% included sexual risk). There were no significant temporal trends in sexual risk for HIV-negative (p=0.888) or HIV-positive (p=0.470) MSM. For HIV-negative MSM, poppers-use decreased over time (p=0.018 for trend) and became a significant risk predictor later in the study (p=0.062 at start compared with OR=1.984, p=0.001 at end). For HIV-negative men, erectile dysfunction drug-use did not change over time (p=0.461) and was consistently associated with risk (OR=2.10, p<0.001). For HIV-negative men, gamma-hydroxybutyrate- (GHB-) and crystal methamphetamine-use remained consistent over time (p=0.231 and p=0.704 respectively); both were associated with risk early in the study period (GHB-use: OR=5.05, p<0.001; crystal methamphetamine-use: OR=6.265, p<0.001), but not at the end (p=0.424 and p=0.196). For HIV-positive men, poppers-, marijuana-, and Ecstasy-use decreased over time (all p<0.01), only poppers-use was associated with risk (OR=1.30, p=0.047), and there were no significant trend interactions with risk.

Conclusions: MSM reported consistent levels of sexual HIV risk over nearly 4 years of follow-up (17% of sexual encounters for HIV-negative MSM and 25% for HIV-positive MSM).

EPHP7.05

Decreasing community viral load (VL) among HIV-positive men who have sex with men (MSM) in British Columbia (BC): 2003-2014

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Background: We examined determinants and trends in the proportion of HIV-positive MSM with unsuppressed VL over 10 years in BC.

Methods: We conducted a retrospective analysis including all HIV-positive MSM from 04/2003 to 03/2014 identified in the provincial STOP HIV database. This database includes: positive HIV test results, antiretroviral therapy (ART) dispensing information, VL and CD4 cell counts, physician billing data, hospital discharge abstracts and vital statistics linkages. For each year, individuals were classified as having an unsuppressed VL if they: 1) were newly diagnosed; 2) had any VL ≥200 copies/ mL measure; or 3) did not have a VL measure (and last VL was ≥200 copies/mL). We examined demographic and clinical factors associated with unsuppressed VL using generalized estimating equations to build a multivariable logistic regression model.

Results: Of 3671 MSM included in the analysis, 87% resided in Vancouver and 78% were Caucasian. The proportion of those with unsuppressed VL decreased from 71% in 2003 to 25% in 2013 (OR=0.77 per year, 95%CI: 0.76-0.78). In multivariate models, having an unsuppressed VL was associated with younger age at diagnosis (aOR=0.94 per 10 year increase; 95% CI 0.90-0.99), Asian compared to Caucasian (aOR=1.29; 95% CI 1.04-1.61), history of injection drug use (IDU) (aOR=1.51; 95% CI 1.34-1.71), testing HIV-negative prior to diagnosis (aOR=1.53; 95% CI 1.38-1.70) and suboptimal ART adherence to therapy (aOR=10.29; 95% CI 9.35-11.33) or not being on ART (aOR=130.66; 95% CI 113.91-149.87) compared with optimal adherence. We found no variation by health authority.

Conclusion: Across BC, the proportion of HIV-positive MSM with unsuppressed VL has fallen as the proportion on those receiving ART has increased. Younger men and those with a history of IDU may require additional support to engage and remain in treatment.

EPHP7.06

Temporal trends in HAART optimism and risky sexual behaviour among HIV-positive and HIV-negative men who have sex with men (MSM) in Vancouver

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Background: Previous analyses have shown that HAART optimism may reduce condom-use among MSM. We examined trends in HAART optimism and risky sex over a three year period within a cohort of MSM in Vancouver.

Methods: We collected demographic and sexual risk behaviour information using a self-administered computer-based survey among sexually active MSM aged ≥16 years from February 2012 to August 2015. The survey included the HAART Optimism Scale (HOS), a 12-item validated instrument (range 12 – 46) for measuring attitudes towards HIV and antiretroviral therapy (ART). We evaluated trends in HOS scores, the proportions of participants reporting condomless anal intercourse with a serodiscordant or unknown serostatus partner in the previous six months (risky sex) and the proportions agreeing with the statement "a person with an undetectable viral load (VL) cannot pass on the virus" by six-month time intervals using generalized estimating equations. All analyses were stratified by self-reported HIV serostatus.

Results: We enrolled 774 participants of whom 556 self-reported as HIV negative/unknown and 218 as HIV positive. The median age was 34 years and 585 (75.6%) identified as Caucasian. The trends regarding risky sex, HAS scores and agreement with the statement are found below.

Conclusions: We observed increasing agreement regarding the preventive value of ART among HIV negative/unknown participants, and increases HAART Optimism Scores for all study participants over a three year period. However, these trends did not correspond with increases in risky sex in either HIV negative/unknown or positive men, which was generally higher among HIV positive men.

HIV negative/unknown							
Time period	**Jul - Dec 12**	**Jan -June 13**	**Jul - Dec 13**	**Jan - June 14**	**Jul - Dec 14**	**Jan - June 15**	**p value**
HAART Optimism Scores (Median)	24	24	25	25	26	26	< 0.001
Agree "undetectable VL cannot transmit" (%)	20	22	26	30	34	36	< 0.001
Risky Sex (%)	30	32	33	29	33	27	0.104
HIV positive							
HAART Optimism Scores (Median)	28	30	28	29	31	31	< 0.001
Agree "undetectable VL cannot transmit" (%)	46	50	44	47	50	55	0.111
Risky Sex (%)	29	43	40	42	46	41	0.656

EPHP7.07

HIV Risk and Prevention Uptake among a Community Sample of Young Gay and other Men Who Have Sex with Men (MSM) and Transgender Women Sex Workers in Thailand

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Background: Young MSM (YMSM) and transgender women (TGW) engaged in sex work (SW) have high occupational exposure to HIV and high HIV-prevalence. We assessed correlates of HIV risk and prevention uptake among YMSM and TGW SWs in Thailand.

Methods: We collaborated with community-based organizations (CBOs) serving YMSM and TGW, including SWs, to conduct venue-based sampling of staff at go-go bars, host bars and massage parlors, and CBO clients, in Chiangmai and Pattaya. Inclusion criteria: gay/MSM- or TGW-identified, 18-30 years-old. We used tablet-administered surveys to assess sociodemographics, SW, HIV-risk and -preventive behaviours, and forced sex. Data were analyzed with Chi-square and Fisher's exact tests, and multiple logistic regression using Stata v.11.2. Based on systematic differences between gay- and TGW- vs. heterosexual- and bisexual-identified participants, we stratified all analyses.

Results: From April-August 2013, we surveyed 408 YMSM and TGW (92.5% RR), 53.4% gay-, 16.7% heterosexual-, 4.4% bisexual-, 25.5% TGW-identified. Overall 41.4% had < high-school education (HSE), 15.2% STI-diagnosis (past year), 21.3% experienced forced sex and 50.5% were HIV-tested (ever). 63.4% engaged in SW. Among gay men/TGW, SW was significantly associated with < HSE, > income, > male partners, > frequent anal sex, receptive-only role, paying for sex, forced sex, and consistent condom use; HSE was associated with 64% lower odds and forced sex 3-fold higher odds of SW. Among heterosexual/bisexual MSM, SW was associated with < HSE, > male partners, sex with women, and perceived risk of HIV; HSE was associated with 89% lower odds and paying for sex 5-fold higher odds of SW.

Conclusion: Preventive interventions should promote access to high-school education and increased HIV testing for YMSM and TGW in Thailand. Tailored interventions for non-gay-identified male SWs should focus on condom use, and risks with female and paid partners, and for gay and TGW SWs reducing incidence of forced sex.

EPHP7.08

Sexual risk reduction strategies among gay, bisexual and other men who have sex with men in Toronto, Canada: A Latent Class Analysis

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Background: Sexual risk-reduction strategies such as refusing condomless anal sex (CAS), or discussing serostatus have been identified as HIV prevention strategies among men who have sex with men(MSM). Using Latent Class Analysis(LCA), we examined patterns of strategies used and factors associated with these patterns.

Methods: Based on the pattern of using five strategies: refusing CAS, seeking information to avoid CAS, discussing HIV status, carrying condoms, and engaging in less risky sexual acts, we calculated posterior probability of a participant being in a risk-reduction class (n=470 HIV-negative Torontonian MSM). We used *Entropy*, the Bayesian information criterion and the Lo-Mendel-Rubin likelihood-ratio-test to identify the best solution. We fit a multinomial regression model to differentiate risk-reduction classes by individual factors.

Results: Fit indices suggested a three class solution. Two-thirds(67%) of the sample reported lower probability of using any strategy, whereas 24% reported higher probability of seeking information to avoid CAS(0.50), discussing HIV status(0.60), carrying condoms(0.75), and engaging in less risky sexual acts(0.77). Further 9% reported higher probability of refusing CAS(1.00) and engaging in less risky sexual acts(0.37). Almost 59% (24/41) of the refusal class and 15% (46/312) the low strategy use class reported no anal sex in the last 90 days, but when they did both classes were more likely (p<0.01) to engage in CAS than MSM in the multiple strategy use class. Low strategy use class MSM were more likely to be younger, non-Hispanic White, single and Canadian born.

Conclusion: LCA identified three classes of MSM based on risk-reduction strategies used, and factors characterizing these classes. Findings show MSM employing multiple strategies is more successful in avoiding CAS than the MSM relying on a single strategy of refusing CAS. Results highlight the importance of going beyond whole-population approaches that obscure differences among MSM, and instead tailoring interventions to an individual MSM's pattern of risk-reduction strategies.

EPHP7.09

Antiretroviral therapy based HIV prevention awareness, acceptability and use among transgender gay and queer men: Findings from interviews in Vancouver, BC

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Disproportionately affected by HIV, gay and queer men are a key target population for antiretroviral therapy (ART)-based HIV prevention. Little is known about the impact of HIV on transgender (trans) gay and queer men and the potential benefits of this intervention among this population. Mixed-method data exploring HIV risk among trans gay and queer men (n=14) were gathered from baseline surveys of an ongoing prospective cohort of gay men with follow-up semi-structured interviews conducted between November and December 2014 (n=11/14, 78.6% response rate). Presented findings focus on participants' narratives of post-exposure prophylaxis (PEP) and pre-exposure prophylaxis (PrEP) acceptability, access, and use. Participants' median age was 26 years [1st-3rd quartile: 24-28], 86% were White and all were HIV-negative. Most participants had at least some knowledge of, two had considered using, and two had used PEP. Most common motives for PEP consideration/use included an unplanned risk event (e.g. condom breakage, sexual assault), HIV-related fear, and as part of a combination HIV prevention strategy. Barriers to PEP consideration/use included both general barriers (e.g., need for a flexible schedule, fear of side effects) and trans-specific barriers (e.g., not using preferred names and pronouns, non trans-inclusive forms and patient record systems). While some participants had heard of PrEP, knowledge was limited overall and none had considered using or had used PrEP. Most had heard of Treatment as Prevention (TasP), and HIV viral load impacted sexual decision-making for a few. Overall, participant narratives indicated awareness of, perceived efficacy of, and a willingness to use PEP, though this is not yet the case for PrEP and awareness of other ART-based prevention varied. As ART-based prevention becomes increasingly integrated into the combination HIV prevention toolkit, policy and programming must take into account the unique needs of transgender gay men as well as those shared with cisgender gay men.

EPHP7.11

Communicating with the community among poor literacy key populations

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Background: Women Sex Workers in India are victims of Poverty, exploitation, trafficking, Gender based violence by family, society and state actors and ignominious stigmatization and social exclusion. This increased their vulnerability to HIV and critical infections and deprived them of human rights and dignity. 74% of estimated 100,000 Sex workers in the state are illiterate and the remaining partially so. This has further diminished their informed choices and enhanced marginalization. Project '*Samvedana*' funded by UNTF and implemented by KHPT addressed Gender Based Violence and its interface with HIV among the FSW in 15 districts of Karnataka, South India.

Methods: Critical engagement of community, in planning, implementation, and monitoring applying Program Science principles to enhance perceptions on violence and capacity building of CBOs to comprehensively address violence and sensitizing stakeholders demonstrated possibilities of proactive addressing and changing equations of Power within and power over.

The strategy involving community in identifying issues, designing communication materials in comic book format with dominant visuals and less text, matching their literacy levels, was evolved.

15 Effective materials were developed. Materials on "Forms of violence, crisis management, impact of violence on their children, Immoral Traffic prevention Act, Fundamental and property rights, , Marriage and Divorce and compensation laws Savings and social entitlements attracted beyond 100% attendance.

Over 1600 community facilitators and 160 master trainers trained 38000 FSWs in large group and campaign mode sessions.

Results: Perception of perpetrators of violence changed significantly.. Identifying Intimate partner violence improved from 27% to 48%. Dominant reasons were maligning, alcohol and Monetary issues

Among the survivors of Violence referred to different services, 95% accessed counseling, 91%accessed STI services, 90%HIV testing, 92%Police, 72% social entitlements.

Conclusion: Proactive involvement of the community in the project cycle ensures achieving objectives and also is a process of empowerment in itself beyond the project.

HIV Program Science
La science dans l'élaboration des programmes sur le VIH

EPHP8.01

Barriers and facilitators of retention in HIV care in high-income settings: A systematic review

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Introduction: Retention in HIV care is an important stage of the HIV care continuum providing opportunities to monitor antiretroviral therapy adherence, prevent HIV-associated complications and deliver ancillary services improving overall survival and reducing HIV transmission risk.

Objective: This review aims to identify barriers and facilitators to retention in HIV care to aid in the development of interventions to increase retention in HIV care in high-income settings.

Methods: Searches were conducted in MEDLINE, EMBASE and PsycInfo in July 2015. Reference lists of included articles were hand-searched. Articles published since 1996 were included. Both quantitative and qualitative studies with retention in HIV care as an outcome were included. Studies focusing on children, youth, transitioning into and out of prison, and transitioning between pre- and post-natal care were excluded. Screening, data extraction, and quality assessments were completed by two independent reviewers. Only quantitative studies with statistically-adjusted data were included in this analysis.

Results: A total of 5,522 citations were identified, of which 73 quantitative studies (5 prospective cohorts, 7 retrospective cohorts, and 61 cross-sectionals) met inclusion criteria. The majority of studies (n=59, 81%) were conducted in the US. Frequently reported barriers to HIV care were: substance use (n=18, 25%), age 18-55 years (n=10, 14%), being on Medicaid or uninsured (n=8, 9%), being African-American (n=6, 8%), and race other than White, Black or Hispanic (n=5, 7%). Frequently reported facilitators to HIV care were: being insured (n=10, 14%), older age (>50) (n=9, 12%), receiving case-management (n=8, 9%), Hispanic/Latino race (n=6, 8%), and being on antiretroviral therapy (n=5, 7%).

Conclusions: The identification of facilitators and barriers to retention in HIV care is a critical first step in designing interventions that are adaptable to local contexts and which provide the greatest chance of successful implementation.

EPHP8.02

Heterogeneity in the emerging trends and patterns of HIV transmission among key populations in Pakistan: a mathematical modeling study of survey data

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Background: Assessing patterns and trends in occurrences of new infections is key to understand HIV epidemics, and is best done through monitoring changes in incidence over time. This study explores trends in the emergence of HIV transmission among key populations(KPs; people who inject drugs[PWIDs], female sex workers[FSWs] and *hijra*/ transgender/male sex workers[H/MSWs]) in several cities of Pakistan.

Methods: A mathematical modelling exercise was performed using four rounds of mapping and surveillance data collected among KPs in each city. Empirical HIV prevalence estimates of each KP in each city at four time points were used to fit models. Prevalence at time points that were not estimated from survey data, and incidence rates per person-years, were then estimated from the models.

Result: In 2010, the estimated incidence rate ranges from 0.0-5.2 in Quetta to 69.1-72.1 in Faisalabad among PWIDs, 1.2-2.4 in Hyderabad to 16.1-18.3 in Karachi among H/MSWs, and zero in Faisalabad to 2.4-4.1 in Karachi among FSWs per 1000 person-years. In 2015, the projected incidence rate ranges from 0.1-6.5 in Quetta to 51.1-55.2 in Faisalabad among PWIDs, 2.5-2.9 in Peshawar to 29.5-40.3 in Karachi among H/MSWs, and zero in Faisalabad to 5.7-8.1 in Larkana among FSWs per 1000 person-years. While the estimated incidence rate among all KPs combined in Pakistan has increased from 11.8-12.7 in 2007 to 15.1-17.0 in 2015, the rate in the general population is likely to be in a range of 0.05-0.07 per 1000 person-years between 2015-2020. The overall trend in HIV prevalence in Pakistan is likely to remain in a range of 0.04%-0.08% between 2015-2020.

Conclusions: Geographical and temporal heterogeneity exists in the emerging trends of HIV transmission, and in the trajectories of prevalence and incidence among KPs in Pakistan. Further study is needed to examine the impact of mixing between sex workers with PWIDs in HIV transmission.

Interdisciplinary Epidemiology (Biological, Behavioural and Social) or Biopsychosocial Research
Épidémiologie interdisciplinaire (biologique, comportementale et sociale) ou recherche biospychosociale

EPHP9.01

Association Between Food Insecurity and Low CD4 Count Among HIV Infected People: A Systematic Review and Meta-Analysis

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Background: While effective antiretroviral treatment can significantly increase CD4 counts in the majority of patients, there are certain populations who remain at relatively low CD4 count levels, and therefore at higher risk for various opportunistic infections. In addition to well know factors such as treatment interruption and non-adherence, food insecurity has been identified as an issue that is associated with lower CD4 counts among HIV infected people. However, studies describing the association between food insecurity and low CD4 count have been inconsistent. Therefore, we aimed to systematically review published literature to determine the association between food insecurity and CD4 count among HIV infected people.

Methods: PubMed, Web of Science, ProQuest ABI/INFORM Complete, Ovid Medline and EMBASE Classic, plus bibliographies of relevant studies were systematically searched through May, 2015. Studies that quantitatively assessed the association between food insecurity and CD4 count among HIV infected people were eligible for inclusion. Study results were summarized using random effects model.

Results: A total of 2093 articles identified through electronic database search and manual bibliographic search, of which 8 studies included in this meta-analysis. Food insecure people had 1.32 times greater odds of having lower CD4 counts compared to food secure people (OR=1.32, 95% CI 1.15-1.53) and food insecure people had on average 91 fewer CD4 cells/µl compared to their food secure counterparts (mean difference=-91.09, 95% CI -156.16, -26.02).

Conclusion: Our summarized estimate indicated that food insecurity is significantly associated with low CD4 count. Therefore, addressing food insecurity may improve immunologic treatment outcomes and help prevent opportunistic infections.

EPHP9.02

Association Between Food Insecurity and HIV Viral Suppression: A Systematic Review and Meta-Analysis

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Background: While early HIV treatment is recommended and effective, many HIV infected people remain untreated, do not achieve complete HIV viral suppression, and remain at risk for AIDS and other related outcomes. Although poor treatment adherence and subsequent drug resistance are known obstacles in achieving HIV viral suppression, food insecurity has been identified as another important issue. However, studies describing the association between food insecurity and complete HIV viral suppression have been inconsistent. Therefore, we aimed to review the published literature to obtain a summary of the relationship between these two factors.

Methods: Electronic databases (PubMed, Web of Science, ProQuest ABI/INFORM Complete, Ovid MEDLINE(R), EMBASE classic) and bibliographies of relevant studies were systematically searched through April, 2015. Studies that quantitatively assessed the association between food insecurity and HIV viral suppression were eligible for inclusion. Study results were summarized using a random effects model.

Results: Twelve observational studies were included (8 cross sectional studies and 4 cohort studies) with a total of 7624 participants. Meta-analyzed results revealed that those experiencing food insecurity had 31% less odds of achieving complete HIV viral suppression compared to those who were food secure (OR=0.69, 95% CI=0.59, 0.81). This significant inverse association was consistently found across different subgroups defined by study design, exposure measurement, and confounder adjustment methods.

Conclusion: Our summarized estimate indicated that food insecurity is significantly associated with incomplete HIV viral suppression. Therefore, addressing food insecurity may improve virologic control, treatment outcomes, and help curtail HIV epidemics.

EPHP9.03

Injection drug use is associated with food insecurity in HIV-HCV co-infected individuals in Canada (CTN264) – a sub-study of the Canadian Co-infection Cohort (CCC)

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Background: In HIV-positive populations, food insecurity (FI) is associated with sub-optimal HIV treatment adherence and adverse health outcomes. Among HIV-HCV co-infected populations, injection drug use (IDU) may be a particularly important risk factor for FI. This longitudinal study examines the relationship between recent IDU and FI among co-infected individuals in the CCC.

Methods: This prospective analysis used data collected biannually from questionnaires (N=642 in 17 centres across 6 provinces, November 2012-March 2015). FI in the past 6 months was measured using Health Canada's Household Food Security Survey Module and categorized as: food secure; marginal, moderate, or severe FI. Recent IDU (in the past 6 months) was self-reported. Multiple imputation by chained equations was used to impute missing observations. Generalized estimating equations were used to estimate the effect of recent IDU on FI in multivariate logistic regression. The dependent variable was a binary indicator: food security vs. any FI. A priori confounder selection was informed by directed acyclic graphs and independent variables were lagged in time to ensure temporal ordering.

Results: Among 642 participants followed for a median of 0.46 years, 31% recently injected drugs and 64% (7% marginal, 23% moderate, 34% severe) experienced FI at baseline. Recent IDU was significantly associated with FI (adjusted OR: 1.39, 95% CI: 1.03-1.89) after adjustment for: age, sex, province, Aboriginal status, housing, education, employment, income, previous IDU (beyond the past 6 months), other substance use (recent alcohol, cigarette, or marijuana use), other modes of recent drug use (snorting), recent anxiety or depression, and self-described health state (visual analogue scale).

Conclusions: Recent IDU is a significant risk factor for FI. Given a high prevalence of IDU, substance abuse treatments and the integration of food supports in harm reduction programs may mitigate FI and its impacts on health in this vulnerable sub-set of the HIV-positive population.

Introducing New Data Sources: Cohort Studies, Administrative Databases, Surveys, etc. Introduction de nouvelles sources de données : études de cohortes, bases de données administratives, enquêtes, etc.

EPHP10.01

A mixed methods study to characterize the organizational attributes of HIV care settings in Canada

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Context: HIV is a complex condition that increasingly requires a shift from a specialist focus to one of primary and preventative health care. Within this shift, we need a better understanding of how care is currently provided to people with HIV and to identify features associated with improved patient care.

Methods: Stage One of this mixed methods study is a cross-Canada survey. We used the validated "Patient-Centered Medical Home Assessment (PCMH-A)" and the CIHI Organizational Attributes of Primary Health Care Survey adapted for the HIV environment, informed by the Primary Health Care HIV Indicator Framework developed by the Living with HIV (LHIV) Innovation Team. We conducted pilot tests in three practices before full implementation.

The survey measures practice attributes (i.e., patient rostering, team composition, organizational support, leadership, level of patient-centered interactions, access and care coordination) and "ingredients" of care (i.e., as human and technical resources, clinic services, attributes, patient populations, etc.).

Results: In Stage One, 43 surveys were sent to clinics in 9 provinces. 21 surveys have been completed (response rate 49%), with survey closure anticipated by mid-February 2016. Descriptive statistics will be generated for each survey domain and all clinical practice characteristics. Chi-squared and t-tests will be used to assess the association between practice characteristics and each patient-centered domain where appropriate. In cases where the data is not normally distributed the Mann-Whitney U test may be used. All differences will be deemed significant at the 5% level. These results will be presented at the conference.

Conclusions: We anticipate our results will help design quality primary care delivery strategies for patients living with HIV, attending to the broader aspects of primary health care.

EPHP10.02

Women with HIV are less likely to receive age-appropriate breast cancer screening compared to HIV negative women: A population-based study in Ontario, Canada

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Background: As people with HIV live longer, they have the same need for age-appropriate cancer screening as the general public. No population-based studies have examined breast cancer screening mammography among women with HIV.

Methods: We conducted a population-based study using Ontario's health administrative databases held at the Institute of Clinical Evaluative Sciences. Screening mammography eligible women were aged 50 to 67 years between April 1, 2011 and March 31, 2013, with no previous breast cancer. HIV status was ascertained using a validated algorithm. We used multivariable log-binomial regression to compare the prevalence of screening by HIV status and to examine the correlates of mammography screening among women with HIV. Results are reported as adjusted prevalence ratios (aPR) with 95% confidence intervals (CI).

Results: Among 1,447,027 women aged 50-67 years, 623 (0.04%) were women with HIV. These women, compared to women without HIV, received screening mammography less frequently (50.1% vs. 63.4%; adjusted prevalence ratio (aPR) 0.80; CI 0.74 to 0.86). After adjustment for patient (age, neighborhood income quintile, immigrant status, and comorbidity) and family physician characteristics (sex, remuneration model and rurality of practice), among women with HIV, women with a female family physician had higher prevalence of receiving mammography (aPR 1.07; CI 0.94

to 1.21), although this finding was not statistically significant. No other patient or physician characteristics were associated with receipt of screening mammography.

Conclusion: Women with HIV in Ontario receive fewer breast screening mammograms than HIV-negative women. Further research is required to determine strategies to improve screening in this population and to understand sub-populations at potential risk for inadequate screening.

EPHP10.03

Cluster Analyses of Physician Visits and Pharmaceutical Dispensations of HIV Positive Individuals Prior to HIV Diagnosis

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Background: Understanding utilization patterns of HIV positive individuals, prior to their diagnosis, can inform earlier diagnosis, engagement and prevention strategies.

Methods: Data were from a population-based linkage study comprising HIV-positive individuals presenting to care between 2007-2011 to the Manitoba HIV Program. Physician visit diagnoses were classified according to International Classification of Diseases chapters. Binary indicators for type of diagnosis and pharmaceuticals dispensed in the 2 years prior to HIV diagnosis were created. Using Stata 11.0, hierarchical cluster analysis was used to find clusters within the study population, based on physician and pharmaceutical utilization. Ward's linkage algorithm was used with the matching coefficient; pseudo T^2 and F statistics determined cluster sizes. Analyses were stratified by sex.

Results: A total of 178 cases were included (118 men, 60 women). Based on physician visits, 5 clusters were found for men, and 4 for women. Among men, 2 clusters were characterized by high physician utilization, with one cluster composed of individuals with multiple morbidities, while the other was marked by a high proportion (67%) having endocrine-system related diagnoses. Another 2 clusters were marked individuals with multiple mental health diagnoses. Low utilization clusters were found for men and women; these clusters contained, on average, the youngest individuals. Using pharmaceutical data, 5 clusters were found for men and women each. One male cluster was characterized by prescriptions for anxiety (86%), depression (71%), mood disorders (86%), and schizophrenia (57%). A similar cluster existed among women, characterized by prescriptions for anxiety (73%), depression (73%), and mood disorders (100%).

Conclusions: Distinct clusters, based on different aspects of healthcare utilization were found. High morbidity, especially mental health issues, were present in HIV-positive individuals prior to HIV diagnosis. The high degree of interaction with the healthcare system prior to diagnosis indicates a need to better understand scope and quality of care.

Methodological Advances in Epidemiology, Public Health and Mathematical Modelling
Progrès méthodologiques en épidémiologie, santé publique et modélisation mathématique

EPHP11.01

Importance of Epidemiological Tipping Point Ratio for ART Programme Success

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Background: The epidemiological tipping point ratio (TPR) of new HIV infections to antiretroviral treatment (ART) initiations has been suggested as a useful indicators to assess if ART scale-up programmes (once coverage exceeds >67%) suffice to control the epidemic. However, this coverage threshold has been disregarded when deriving TPR to rank programmes across countries. Our study aims to assess i) how changes in TPR impact the HIV epidemic and the likelihood of HIV elimination, and ii) validity of TPR as indicator of ART progress across settings.

Methods: We used a dynamic model of HIV transmission informed by South African epidemic data to simulate ART scale-up scenarios yielding TPR between 0.5 and 2. We compared ART coverage and HIV incidence across different ART eligibility thresholds and epidemic conditions.

Results: With early ART initiation (i.e. CD4<500 or <350 cells/μL), scaling-up ART and reaching TPR=1 can theoretically lead to HIV elimination, unlike when TPR=1 is reached by initiating ART late (i.e. CD4<200). High ART coverage reached by early initiation achieves and maintains low TPR and reduces HIV incidence substantially. Late initiation leads to initially low TPR which plateaus slightly below 1, reflecting modest ART coverage (~60%) and limited incidence reduction. Furthermore, such reduction is not directly related to TPR: TPR<1 can have smaller impact than TPR>1 across settings.

Conclusion: In HIV surveillance, the TPR does not fully indicate programme impact or elimination likelihood without further information on ART coverage and ART eligibility threshold. Such data is important when comparing progress towards elimination across countries.

Reduction in annual HIV incidence (relative to no intervention scenario) and ART coverage (i.e. % of all HIV+ individuals on ART) at 50 years after the beginning of ART scale-up

Eligibility, Setting	ART programme TPR target				
	0.50	0.80	1.00	1.25	2.00
	% incidence reduction / % ART Coverage				
CD4<200, A[1]	71 / 57	71 / 57	69 / 55	63 / 49	49 / 37
CD4<350, A[1]	97 / 81	92 / 69	88 / 62	82 / 55	68 / 41
CD4<500, A[1]	98 / 84	94 / 72	91 / 65	87 / 58	73 / 43
CD4<200, B[1,2]	70 / 49	70 / 49	70 / 49	69 / 48	54 / 36
CD4<350, B[1,2]	98 / 76	96 / 71	92 / 63	86 / 55	68 / 40
CD4<500, B[1,2]	99 / 88	97 / 75	94 / 67	88 / 59	70 / 42
[1]Setting A&B: 11% baseline HIV prevalence at the start of ART scale-up.					
[2]Setting B = Setting A +40% partner acquisition rate, +40% population growth rate.					

EPHP11.02

Do Modelling Assumptions About HIV Disease Progression On and Post-treatment Affect Estimates of Treatment Impact?

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Background: Many mathematical models have investigated the potential epidemiological impact of expanding antiretroviral therapy (ART) coverage, using very different assumptions about HIV disease progression for people on ART and those who drop out of ART. We evaluated the effect of these different assumptions on 10-year model impact projections.

Methods: A model of HIV transmission among men who have sex with men (MSM) in the United States was developed, with four different previous assumptions about disease progression investigated in turn: (A) slower CD4 decline on vs. off ART; (B) no CD4 change on ART; (C) CD4 increases on ART; (D) CD4 increases upon stopping ART with faster CD4 decline for ART dropouts vs. ART naïve. The model was fit to data for American MSM under each assumption and the proportion of HIV infections averted was compared for the same increases in ART coverage (between 12-57%).

Results: Across different assumptions, mean survival for ART patients and ART dropouts varied between 32.1-47.7 and 6.4-8.8 years, respectively. When ART dropouts re-initiated ART at the same rate as ART-naïve MSM, little variation in impact of increased ART coverage was seen between assumptions (<5% absolute difference between 10-year projections of proportion of HIV infections averted). Differences remained small (<5%) for different baseline ART dropout rates, HIV prevalence, and ART coverage. Achieving the same increase in ART coverage by decreasing ART dropout rates rather than increasing ART uptake gave smaller and slightly more divergent impact projections. If ART dropouts were assumed to reinitiate ART only at CD4<200 cells/µl, (e.g. due to symptoms), assumption (C) predicted substantially more infections averted over 10 years than other assumptions.

Conclusion: Different model assumptions about HIV disease progression on and post-ART produced little variation in 10-year impact projections for expanded ART coverage, unless ART dropouts only reinitiated ART at low CD4 counts.

EPHP11.03

HIV intervention impact predictions from deterministic and individuals based models

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Mathematical models that inform HIV intervention programs often represent interventions in details but oversimplify sexual contact structure that has been shown to influence HIV spread. Whether this affects intervention impact estimates when calibrated to data has never been assessed systematically.

We developed two comparable HIV transmission dynamics models (individual-based(IBM), deterministic(DM)), allowing the IBM to represent different concurrency level, partnership duration, plausible sexual behaviours and HIV prevalence. Two interventions were simulated: a) biomedical resulting in 50% reduction in HIV infectivity, b) behavioural resulting in 50% reduction in partner acquisition rates & dissolution of 50% of existing partnerships. Impacts were measured as the number of HIV infections averted over five years of intervention. First, we compared impact estimates between the DM and IBM for parameter sets matched to give the same total number of partners, sex-acts per individual/year, HIV prevalence/incidence, using the ratio of infections averted within each pair of models. Second, uncertainty in data was addressed by fitting each model to a similar HIV prevalence data estimate (varying key parameters over fixed prior range), and these impacts were compared across models (pragmatic comparison).

In matched comparison, models predicted similar impact of each intervention for short partnership durations (mean<2 years) or in presence of concurrency. The IBM predicted more pessimistic biomedical impact prediction when only allowing long-term sequential partnerships (i.e. no concurrency) (~2-fold less impact for duration >10 years), as infections within couples were merely delayed. When sequential partnerships exceeded 2 years duration, breaking-up partnerships in a behavioural intervention in-

creased the number of serodiscordant partnerships, leading to more infections. In pragmatic comparisons models produced more comparable results.

IBM and DM predicted similar intervention impact except for populations with long sequential partnerships durations and little concurrency. If models adequately reflect the uncertainty in data, these differences may have limited practical implications for decision-making.

Social Determinants of HIV Prevention, Risk, Testing, and Care
Déterminants sociaux de la prévention, du risque, du dépistage et des soins concernant le VIH

EPHP13.01

Voluntary HIV testing: Factors associated with repeated HIV testing among a sample of HIV-negative gay and bisexual men living in Toronto, Ontario

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Background: Over half of new infections in 2011 in Ontario were attributable to gay and bisexual men (GBM). Routine HIV testing remains the sole method to detect infection early and initiate treatment. In Ontario, testing is available at no cost, and can be completed anonymously. We explored factors associated with voluntary (not work/ immigration mandated) HIV testing frequency in GBM in Toronto, Ontario.

Methods: Data from 470 HIV-negative GBM at baseline, 3-month, and 6-month follow-up were collected. Considering demographic, psychosocial, sexual behaviours and enabling (e.g. income) factors in separate blocks, multinomial models estimated bivariate relative risks of each factor, as well as in blocks. The final model included significant ($p<0.10$) factors from all models combined.

Results: Nine percent reported never testing, 58% once, and 34% more than once. In the demographic block, greater age was associated with being a repeated tester compared to never having tested. In the final multinomial model, greater income was associated with having testing once, compared to never testing. Being more open with others about one's sexual orientation, and higher income were associated with being a repeated tester compared to never having tested. Greater social support from friends, having had serodiscordant condomless anal sex (SDCAS) with a male partner in the prior 90 days, were associated with being a repeated tester, compared to a one-time tester, whereas being in a long-term relationship was associated with a decreased likelihood.

Conclusion: Considering the final model controlled for SDCAS, our findings highlight factors to consider when promoting HIV testing. Notably, in a health care system where HIV testing is available at no cost, in various settings, lower income acts as a barrier to testing. Our results also suggest potential for renewed efforts for HIV testing promotion in younger GBM and couples-based testing for men in relationships.

EPHP13.02

Place Matters: Key Findings of a Scoping Review on HIV point-of-care testing (HIV POCT) in Non-urban Settings

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Background: HIV point-of-care testing is an innovation that can allow for counseling, testing and reporting of test results to be conducted in the same visit. This approach can be highly useful in non-urban locations where centralized testing services may not be accessible. To better understand the current state of providing HIV POCT in non-urban locations in Canada, we undertook a scoping review of the peer-reviewed literature to explore how place matters.

Methods: For the purpose of this scoping review, non-urban settings were defined according to the 2013 OECD Regions at a Glance database, or were self-described as non-urban or rural by the study authors. We searched Ovid MEDLINE, including In-Process and Other Non-Indexed Citations (1946 to 3rd week August 2014), EMBASE (1974 – 25 August 2014), EBM Reviews (1991 – 3rd Quarter 2014), PsycINFO (1806 – 25 August 2014), and CINAHL (1980 – 25 August 2014). A total of 3,142 studies were identified, and a total of 18 met our inclusion criteria. Of these, 12 studies evaluated HIV POCT programs in non-urban settings, whereas 6 studies elicited opinions about POCT in non-urban settings or at innovative sites.

Results: Non-urban HIV POCT programs were implemented and evaluated in community health centres, door-to-door outreach, hospital, pharmacy, primary care settings, prisons, and substance abuse clinics. The potential feasibility and acceptability of HIV POCT were highlighted in diverse sites such as dental offices, home testing, community pharmacies, primary care settings, and sexual health/ HIV clinics.

Conclusions: Innovative approaches and non-traditional models of HIV POCT have a number of public health benefits that are particularly relevant in rural or non-urban settings. However, testing innovations such as HIV POCT in non-urban settings warrant additional implementation research in order to understand how best to scale up novel approaches where equitable access to HIV testing does not exist.

EPHP13.03

Social and Structural Factors Associated with Greater Time Above an HIV Viral Load of 1500 Copies/mL Plasma among Illicit Drug Users in a Canadian Setting

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Background: Although previous studies have characterized temporary increases in plasma HIV-1 RNA viral load (VL) among HIV-positive people who use drugs (PWUD), factors associated with longer periods of time with heightened HIV transmission potential have not been investigated. Therefore, we examined factors associated with amount of person-time spent above a VL threshold that increases risk of transmission to others among HIV-positive PWUD in Vancouver, Canada.

Methods: Data were derived from the AIDS Care Cohort to evaluate Exposure to Survival Services (ACCESS), a long-running prospective cohort of HIV-positive PWUD linked to comprehensive clinical monitoring records. We used Poisson regression to longitudinally examine factors associated with person-time (in days) above a VL of 1500 copies/ml in the previous 180 days.

Results: Between December 2005 and May 2014, 845 participants were included in the study, including 581 (69%) males and 464 (55%) who self-reported Caucasian ancestry. Of these, 593 (70%) spent at least one day with a VL above 1500 copies/ml during the study period. In a multivariable model, homelessness (Adjusted Rate Ratio [ARR] = 1.50; 95% confidence interval [CI]: 1.36 – 1.65), and having no social support (ARR = 1.36; 95% CI: 1.23 – 1.49) were independently and positively associated with amount of time spent over 1500 copies/ml. Age (ARR = 0.97; 95% CI: 0.97–0.98), enrollment in addiction treatment (ARR = 0.73; 95% CI: 0.65–0.82), and CD4 cell count (ARR = 0.81; 95% CI: 0.78 – 0.85) were independently and negatively associated with time spent over 1500 copies/ml.

Conclusions: Among HIV-positive PWUD, periods of homelessness or lacking in social support were independently associated with greater time experiencing an elevated VL. Our findings suggest the need for targeted prevention efforts to address modifiable factors associated with risk of HIV transmission among PWUD.

EPHP13.04

Socio-economic, Clinical and Behavioural Factors Associated With Late Initiation of Antiretroviral Therapy in British Columbia (BC)

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Background: We examined factors associated with late initiation of ART among individuals living with HIV in British Columbia (BC).

Methods: From December 2013 until December 2015, we recruited treatment-naïve individuals who initiated ART within the previous year. Participants completed a structured survey on their demographics and use of healthcare and support services. Clinical variables were obtained via linkage to the provincial HIV/AIDS Drug Treatment Program (DTP). We defined 'late initiation of ART' as CD4 count ≤500 cells/μL at time of initiation. Bivariate analyses tested the association between late initiation and socio-economic characteristics. Logistic regression was conducted to model late initiation, with backward selection and AIC minimization.

Results: We enrolled 89 individuals, of whom 17 (19.1%) were female, 47 (52.8%) were Caucasian, and 14 (15.7%) were of Indigenous ancestry, with a median age of 40 years (1st-3rd quartile (Q1-Q3): 29-46). Participants' median annual income was $13,200 (Q1-Q3: 7,320-28,800). In addition, 20 (22.5%) had ever been incarcerated, 26 (29.2%) had ever used injection drugs and 44 (50%) initiated ART with CD4 counts ≤500 cells/uL (Q1-Q3: 245-650).

In multivariable analysis, individuals with higher monthly income (adjusted odds ratio (AOR): 0.94, 95% confidence interval (CI): 0.90-0.99, per 100 increase), and with a history of homelessness (AOR: 0.13, CI: 0.03-0.51) were less likely to initiate late. Older individuals (AOR: 1.12, CI: 1.05-1.19) and those who reported difficulties taking ART medication related to pill burden (AOR: 5.31, CI: 1.06-26.53) were more likely to initiate late. We did not observe any significant differences in attitudes towards ART and CD4 cell count at time of ART initiation among study participants.

Conclusions: In this analysis, we observed disparities among individuals initiating ART by income, history of homelessness, age, and difficulties taking ART. These results indicate that additional supportive services are needed to alleviate barriers to ART uptake in BC.

EPHP13.05

Rurality is associated with an increased likelihood of readmission to hospital within 30 days among individuals living with HIV

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Background: The unique challenges of geographic isolation faced by rural individuals can negatively affect their health outcomes, and hospital readmission rates are an important health indicator. This study assessed the impact of rurality on the risk of hospital readmission within 30 days among people living with HIV (PLWH) compared to a random sample of the general population of British Columbia (BC).

Methods: Retrospective population data from the Comparative Outcomes and Service Utilization Trends (COAST) study was used to capture all hospitalizations within BC with a discharge date between April 1, 2001 and March 1, 2013. Readmissions included any re-hospitalization within BC occurring within 30 days of an index hospitalization discharge date. Individuals were classified as rural, suburban, or urban using the Statistical Area Classification. Generalized estimating equation modelling was used to evaluate the relationship between rurality and 30-day readmission among PLWH and the general population of BC.

Results: Of 157223 individuals, 150447 were from the general population [91609 (60.9%) urban, 34647 (23.0%) suburban, 21501 (14.3%) rural, and 2690 (1.8%) unknown], and 6776 were PLWH [5391 (79.6%) urban, 860 (12.7%) suburban, 421 (6.2%) rural, and 104 (1.53%) unknown]. Overall, after adjusting for age, sex, Charlson Comorbidity Index, length of admission, ICU admission, and discharge against medical advice, both suburban (adjusted odds ratio (AOR) 1.16; 95%CI: 1.13-1.19) and rural (AOR 1.42; 95%CI: 1.38-1.46) individuals had higher odds of all-cause 30-day readmission compared to urban individuals. Among PLWH, rurality remained associated with all-cause 30-day readmission (rural AOR 1.43; 95%CI: 1.20-1.70) after additional adjustments for antiretroviral use, injection drug use, Indigenous ancestry, baseline viral load, and baseline CD4 count.

Conclusion: Rural individuals are more likely to be re-admitted to hospital. Further research is needed to identify strategies, such as improved discharge planning and ambulatory continuity of care, aimed at reducing readmissions in this population.

EPHP13.06

Differences in Sexual Behaviour and Access to ART are Insufficient to Explain Racial Disparities in HIV Risk for Men Who Have Sex with Men (MSM) in Baltimore

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Background: HIV prevalence in Baltimore, United States, is much higher among black men who have sex with men (MSM) than white MSM (48 vs. 16% in 2011). It is hypothesised that this prevalence difference is driven/maintained by assortative mixing by race and/or differences in antiretroviral therapy (ART) access. We used mathematical modelling to explore these hypotheses.

Methods: A dynamic age- and race-stratified model of HIV transmission and treatment among MSM in Baltimore was parameterised using Baltimore-specific behavioural data and national-level testing data. The model was run using 500,000 randomly sampled parameter sets (varying many parameters including race-specific rates of joining and leaving the MSM population) and multiple fits were found to Baltimore-specific demographic and ART coverage trends and overall MSM HIV prevalence between 2004 and 2011. In further univariate and bivariate analysis using these fits, the levels of race-related mixing and treatment access were varied to identify when the model could also replicate race-specific HIV prevalence.

Results: Neither differences between numbers of sexual partners reported by black and white MSM in Baltimore nor large (>2-fold) differences in access to ART by race were sufficient to replicate observed HIV prevalence disparities. Highly assortative mixing by race (>95% of black MSM partners are black, >82% of white MSM partners are white) was able to reproduce racial prevalence disparities only if black MSM also had higher (>1.6-fold) HIV prevalence than white MSM early in the epidemic. This level of assortative mixing is only slightly higher than reported levels for Baltimore (93%/82% same-race partners for black/white MSM).

Conclusion: Racial disparities in access to HIV treatment were not sufficient to explain the large difference in HIV prevalence seen between black and white MSM in Baltimore. Highly segregated mixing by race could have maintained, but not generated, the observed prevalence difference; alternative hypotheses should be explored.

EPHP13.07

Social Determinants of Delaying Initiation of Antiretroviral Therapy Beyond One Year After HIV Diagnosis

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Background: We examined socio-economic and clinical factors associated with delayed ART initiation among individuals living with HIV in British Columbia.

Methods: From December 2013 until December 2015, we enrolled treatment-naïve individuals who initiated ART within the previous year. Participants completed a survey on demographics, adherence behaviours, and use of healthcare and support services. 'Delayed ART initiation' was defined as initiating ART >1-year following HIV diagnosis. Bivariate analyses and logistic regression analysis modeled the association between delayed initiation, survey responses and clinical characteristics, with backward selection and AIC minimization.

Results: We enrolled 89 participants of whom 17 (19.1%) were female, 47 (52.8%) were Caucasian and 28 (31.5%) were of Asian or other non-Indigenous ethnicity, with a median age of 40 years (1st-3rd quartile (Q1-Q3): 29-46). The median time between HIV diagnosis and ART initiation was 3 months (Q1-Q3: 1-21), with 63 (71.6%) initiating ART ≤1-year following HIV diagnosis.

In bivariate analysis, compared to physician advice to initiate ART immediately, individuals given other advice by a physician (28% versus 4.8%, p-value 0.012) and individuals with a history of incarceration (36.0% versus 15.0%, p-value 0.048) were more likely to delay ART initiation. However, these variables were not selected in multivariable analysis.

In multivariable analysis, compared to married, steady or common-law partnership, individuals with single, dating, widowed, separated or divorced relationship status (adjusted odds ratio (AOR): 0.20, 95% confidence interval (CI): 0.06-0.64) and "other" sexual orientation (queer, bisexual, two spirit, and questioning) (AOR: 0.12, CI: 0.02-0.88) compared to heterosexual orientation were less likely to delay ART initiation. Individuals who reported Asian or other (A0R: 4.87, CI: 1.29-18.42) compared to Caucasian ethnicity were more likely to delay initiation.

Conclusions: The majority of participants initiated ART within 1-year of HIV diagnosis, however disparities in timely ART uptake were observed by relationship status, sexual orientation and ethnicity.

EPHP13.08

Point of Care Testing: Reaching Street Involved People in Ottawa and Winnipeg

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Current approaches to HIV testing in Canada fail to reach a large portion of the population – approximately 25% of HIV positive Canadians are unaware that they have contracted the disease. Canada needs testing strategies that successfully engage high risk people in repeated HIV testing. POC testing employs a rapid finger-prick HIV test that is minimally invasive, fast and easy to transport. The short wait time for results and the opportunity to bring HIV testing outside of the clinic offers an opportunity to increase testing, particularly among marginalized communities such as street involved people. Despite the potential, several Canadian provinces do not offer this form of HIV testing. Furthermore, little research in Canada has focused on POC testing in high-risk, marginalized populations.

This study investigates the acceptability of rapid POC testing among street involved people in Winnipeg and Ottawa. Participants in the Winnipeg and Ottawa Social Network Studies were offered POC testing at a convenient location of their own choosing. Participants were recruited through respondent driven sampling (RDS) and demographic, social network, and behavioural data were collected. RDS recruitment chains were used to investigate testing behaviour among acquaintances. Study participants were asked a series of questions about their experience with POC testing to investigate acceptability.

Participants' opinions of rapid POC testing were overwhelmingly positive. Test uptake was 80.9% in Winnipeg and 85.8% in Ottawa among eligible participants. A significant association was found between the participant's testing behaviour and the testing behaviour of their recruiter. Although many participants reported feeling anxious about the testing process, the majority felt confident in the test results. Notably, more than 95% of participants in each city said would choose a rapid HIV test in the future. These findings offer valuable insight for increasing testing among high-risk populations.

Social Epidemiology of HIV Infection (Structural, Social and Individual Determinants) Épidémiologie sociale de l'infection au VIH (déterminants structurels, sociaux et individuels)

EPHP14.01

The Positive Plus One Project: A national mixed-methods study of risk management, health and wellbeing for people living with HIV and their HIV-negative partners

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Background: As HIV rates have stabilized, HIV-positive individuals are living longer lives, and more people are involved in HIV-serodiscordant relationships. Many diseases and issues bring stress to a relationship, but the impact of HIV is unique due to the ongoing risk of HIV transmission between partners, stigma, and rapidly changing treatment. The Positive Plus One project is the first Canadian national study that aims to provide crucial new evidence about these issues.

Objectives: Positive Plus One aims to: characterize HIV-serodiscordant relationships across Canada; examine the individual, dyadic, and social determinants of relationship satisfaction; examine links between relationship quality and HIV transmission risk; assess partners' needs and access to supportive services; and document how serodiscordance affects everyday life.

Description: Positive Plus One, funded by CIHR and developed in partnership with 31 ASOs /NGOs, clinicians, and researchers, leverages the advantages of quantitative and qualitative social science to collect data from HIV-positive and HIV-negative partners engaged in serodiscordant relationships. Standardized online/telephone surveys (n=2050) will provide an understanding of the dynamics of serodiscordant relationships. Qualitative interviews with a sub-sample of participants will enable us to understand how these relationships unfold over time, and contextualize our findings in participants' lived experiences.

This study is unique because we will analytically link both partners in a dyad. Individuals in current or recent serodiscordant relationships are being recruited, and will then be asked to invite their serodiscordant partners to complete a separate survey/interview. A multipronged recruitment strategy, using traditional methods and social media, is being used to reach LGBTQ and heterosexual couples across Canada and in diverse cultural communities.

Future Directions: Study findings will increase overall levels of health and wellbeing among HIV-serodiscordant couples in Canada by informing policy development and assisting stakeholders in developing new programs and interventions for serodiscordant partners.

EPHP14.02

An Event-Level Analysis of Condomless Anal Sex among Gay, Bisexual, and Other Men who have Sex with Men (GBM) with Online-met Partners

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Background: Meeting sexual partners online has been identified as a risk factor for condomless anal sex (CAS). However, little is known about social predictors of CAS among GBM. Our objectives were to identify predictors of event-level CAS with online-met partners.

Methods: Our prospective cohort recruited sexually-active GBM aged ≥16. Follow-up occurred every six months where participants reported their most recent sexual encounter with their five most recent sexual partners. Social predictors included the number of GBM they were "close to", Collective Self-Esteem scale scores, and two Principal Component Analysis scores assessing Sociality (i.e., social time with GBM, gay bar/club attendance, gay sports team participation) and Community Engagement (i.e., gay-specific group participation, gay pride participation, gay media consumption). Demographic, attitudinal, and event-level factors were also considered. Stratified by participant HIV-status, covariates of event-level CAS (vs. none) with partners met online were modeled using generalized estimating equations to construct hierarchical logistic regression (within participant, within visit).

Results: Of 538 HIV-negative and 211 HIV-positive GBM, 76.0% were white, and 84.9% were gay-identified, with a median age of 33 years. Data were collected on 8137 sexual events of which 4061(49.9%) included an online-met partner, reported by 558 individuals. Multivariable results showed that after controlling for demographic, attitudinal, and event-level factors CAS was predicted by higher Collective Self-Esteem (aOR=1.07, 95%CI[1.01,1.12]), being "close" to more GBM (aOR=1.03, 95%CI[1.01,1.06] per 10 men), lower Gay Sociality (aOR=0.91, 95%CI[0.82,1.00]), and lower Communal Sexual Altruism (aOR=0.57, 95%CI[0.47,0.69]) for HIV-negative men. While, for HIV-positive men, Communal Sexual Altruism (aOR=0.61, 95%CI[0.48,0.78]) was the only significant social factor on either the univariable or multivariable level.

Conclusion: Our findings suggest that sexual altruism, gay sociality, collective self-esteem, and community connectedness have mixed effects on CAS risk, highlighting the need for further research on how social factors, norms, and motivators are shaped in social/peer networks.

EPHP14.03

Resilience in Aging: Shaping Resiliency through a Supportive Housing Intervention

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Background: Adding to the daily challenges of living with HIV, unstably housed people living with HIV/AIDS (PHA) face numerous barriers to achieving optimal therapeutic outcomes. As PHA age, psychosocial and age-related comorbidities further impact disease management. Resiliency can mitigate some of these challenges, particularly through community and social supports. This analysis examines factors associated with high resiliency among a cohort of PHA.

Methods: The study sample consisted of PHA ≥18 years of age enrolled in a longitudinal cohort of PHA at risk of homelessness living in an HIV-specific supported housing facility in Vancouver, Canada. The impact of the housing intervention on residents' quality of life and HIV treatment outcomes were evaluated. Peer-administered surveys collected demographic and socio-behavioural data and were linked with clinical data. Resilience was measured using the validated RS-14 scale and dichotomized as "high" vs. "low." Univariable analyses and multivariable logistic regression were conducted to identify clinical characteristics and selected survey responses associated with high resilience.

Findings: Our analytic sample of 88 participants included 18 (20.5%) females and 32 (36.8%) people of Indigenous ancestry, with median age at 51 (Q1-Q3: 48-57). Overall, 71.6% of participants scored "high" on the resiliency scale. Univariable analyses showed that participants who scored "high" resiliency were significantly more likely to report a history of homelessness, sub-optimal adherence to antiretroviral treatment in the year prior to interview (<95% of prescribed medication), and be older. In multivariable analysis, independent predictors of high resiliency were suboptimal adherence compared to optimal adherence (adjusted Odds Ratio [aOR]=3.45; 95% Confidence Interval [CI]=1.15-10.42) and older age (aOR=1.09; 95% CI= 1.01-1.17).

Conclusion: Results suggest this supportive housing intervention may have a greater relative impact on the resilience of PHA who have experienced more severe socio-structural inequities. Additional analyses are needed to understand how resilience shapes HIV-related health outcomes in aging PHA.

EPHP14.04

The Community Pop-Up Clinic As a Tool of Engagement for Vulnerable Populations with HIV and HCV Infection

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Background: The Downtown East Side Vancouver (DTES) is known for HIV and HCV infection high prevalence. Despite available services, significant numbers remain undiagnosed or unengaged in care. There is a need to develop innovative structures to address this issue and understand the level of HIV infection knowledge and interest to seek care.

Methods: Participants were evaluated at community pop-up clinics (CPCs) held at DTES sites (including InSite, the only supervised injection facility in North America), frequented by meal, shelter or other services. HIV and HCV point-of-care testing was offered with access to our multidisciplinary program. Participants also completed targeted questionnaire for demographic information, HIV infection knowledge and desire to receive care. A $10 incentive was offered for participation.

Results: Since 01/14, 911 individuals (mean age 46.3, 75.3% male) were tested, with 306 (33.6%) infected with HCV infection and 30 (3.3 %) co-infected with HIV. Of 475 PWID, 264 (55.6%) were infected with HCV, and 26 (9.8%) co-infected with HIV. Of these 79 (10 with HIV infection) were not previously known to be infected. Participants identified HIV transmission as occurring through casual contact (17.5%), unprotected sex (55.8%), sharing needles (75.8%), sharing injection equipment (52.9%), or blood transfusion (63.1%). Only 67.5% were aware of HCV infection cure, and 78.5% would consider treatment for it.

Conclusions: Despite the DTES widespread availability of HIV and HCV services, our program identified 79 and 10 new cases of HCV and HIV infection and offered individuals the opportunity to engage in care. There is a significant gap in HIV transmission knowledge, but general willingness to receive care in this population. Innovative low-

threshold programs may be a tool to address HIV and HCV infection in this population.

EPHP14.06

Sexual Event-Level Analysis of Age-Disparate Partners Among Gay, Bisexual and other men who have sex with men (GBM) in Vancouver

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Background: Age-disparate sexual partnerships may drive the HIV epidemic among GBM. We identified factors associated with GBM's older and younger sexual partners in Vancouver.

Methods: Participants were GBM aged ≥16 years recruited from 2012-2014. Participants completed a computer-assisted self-interview reporting on their last sexual event with their five most recent partners. Explanatory factors included demographics, attitudes (e.g., McKirnan's 2001 Escape Motives, study α=0.90), relationship factors, substance use, and sexual behavior (e.g., high-risk sex = condomless anal sex with a serodiscordant/unknown HIV-status partner). Two generalized linear mixed models using multivariable ordinal logistic regression identified factors associated with partners who were 1) "same-age" (referent), "younger" or "much-younger", and 2) "same-age" (referent), "older", or "much-older". Statistical interactions between age and HIV status were tested.

Results: Participants (n=719) were predominantly gay (85.1%), White (75.0%), HIV-negative/unknown status (72.9%) with a median age of 33 (Q1,Q3:26,47). Of 2513 sexual-events reported, 7.4% were with much-younger, 6.4% with much-older, and 35.3% with same-aged partners. GBM were more likely to engage in high-risk sex with older-partners (AOR=1.38,95%CI:1.02-1.87), which was not associated with younger-partners (p=0.20). GBM who reported older-partners were more likely to be gay-identified (AOR=2.74,95%CI:1.54-4.86), Asian versus White (AOR=2.01,95%CI:1.31-3.08), report greater Escape-Motives scores (AOR=1.02,95%CI:1.00-1.05), have partners who report event-level erectile dysfunction drug-use (EDD) (AOR=4.64,95%CI:2.49-8.64), report event-level receiving money, goods and/or drugs for sex (AOR=4.18,95%CI:2.48-7.03), and less likely to report event-level alcohol- (AOR=0.68,95%CI:0.53-0.88) and EDD- (AOR=0.46,95%CI:0.26-0.83) use. Reporting younger-partners was positively associated with an income of >$30,000/year (AOR=1.75,95%CI:1.25-2.47) and having met a partner online (AOR=1.54,95%CI:1.09-2.19). Younger HIV-positive GBM were more likely to be with older-partners (AOR=0.92,95%CI:0.89-0.95) than younger HIV-negative GBM (AOR=0.96,95%CI:0.94-0.98) while older HIV-negative GBM were more likely to be with younger-partners (AOR=1.10,95%CI1.08-1.12) than older HIV-positive GBM (AOR=1.06,95%CI:1.03-1.10).

Conclusions: Discrepancies reported in sexual HIV-risk and transactional sex among age-disparate partners highlight important targets for health promotion and future research.

EPHP14.07

The prevalence and correlates of incarceration experience among women living with HIV in Canada

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Background: HIV disproportionately affects incarcerated women in Canada where the incidence rate is higher than among incarcerated men. We describe the prevalence and correlates of incarceration experience among women living with HIV (WLWH) in Canada.

Methods: We analyzed baseline survey data for 1,425 WLWH ≥16 years, enrolled in the Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS), a prospective, community-based research study in British Columbia (BC), Ontario and Quebec. Prevalence of incarceration experience (Yes vs. No) was assessed via responses to: "Have you ever been incarcerated, or held in custody overnight or longer, in Canada?" Those with invalid responses were excluded (n=3). Multivariable logistic regression examined independent correlates of incarceration experience.

Results: Of 1,422 participants, median age was 43 years (IQR: 35-50), 41% identified as Caucasian, 29% as African, Caribbean or Black-Canadian, and 22% as Indigenous. Prevalence of incarceration experience was 37% nationally, with significant differences by province (62% BC; 29% Ontario; 27% Quebec;p<0.001). In multivariable analyses, significant factors independently associated with incarceration experience included being in any form of government care as a child (AOR=3.01 [95% CI:1.80-5.02]); experiencing violence as an adult (AOR=2.86 [95% CI:1.33-6.20]); reporting higher HIV-related stigma (AOR=1.73 [95% CI:1.10-2.70]); and Hepatitis C co-infection (AOR=3.74 [95% CI:2.14-6.55]). Additionally, women with incarceration experience were more likely to be currently engaged in sex work (AOR=5.44 [95% CI:1.21-24.4]), currently using recreational (AOR=7.74 [95% CI:4.10-14.6]) or injection drugs (AOR=2.76 [95% CI:1.46-5.22]), and less likely to have

received HIV medical care in the past year (AOR=0.27 [95% CI:0.09-0.82]).

Conclusions: Over one-third of WLWH in CHIWOS reported incarceration experience. Results reveal a high burden of social and structural inequities amongst previously incarcerated WLWH. Poor rates of linkage to HIV medical care suggest an urgent need for women-centered prison outreach services to support women returning to communities and to HIV care retention.

EPHP14.08

Comparison of Antiretroviral Treatment Interruptions Between Urban and Rural Populations with HIV Infection in British Columbia

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Introduction: People living with HIV/AIDS (PLWH) in rural areas may have worse engagement across the continuum of HIV care. No comparative data exists on the frequency and impact of antiretroviral therapy (ART) treatment interruption (TI) between urban and rural populations in Canada.

Methods: All ART-naïve individuals (≥19 years) initiating ART between 2000 and 2014 through the BC Drug Treatment Program were included in a retrospective evaluation of TI. TI was defined as a period of >90 days without ART. Degree of rurality was classified using the Statistical Area Classification. Frequency, time to first occurrence, and duration of TI was determined for urban and rural populations. Poisson regression modeling was used to assess the relationship between rurality and TI among PLWH.

Results: Of 3670 eligible individuals (82.3% male), 814 (22.2%) experienced a TI. The majority of individuals resided in urban communities (94.8% Urban, 2.2% Suburban, 3% Rural). Individuals in rural (RR 1.41, 95% CI: [1.05-1.89]) and suburban (RR 1.53, 95% CI: [1.11-2.11]) communities were at increased risk of TI. Kaplan Meier analysis revealed that time to first TI was shorter in participants living in rural and suburban communities. There was no significant difference in median duration (days) of TI based on rurality (Urban 191, Suburban 225, Rural 169 days; p = 0.78).

Conclusions: PLWH in BC experience high rates of TI. Individuals in rural and suburban communities are at increased risk of experiencing TI compared to urban counterparts. Strategies to support sustained ART are needed, particularly for individuals living outside urban communities.

Epidemiology and Public Health Other
Épidémiologie et santé publique, Autre

EPHP15.01

Practice guidelines in peer health navigation for people living with HIV: Guideline development process

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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 convened a 15-member national expert working group made up of researchers, clinicians, public health practitioners, program planners, frontline service providers and people living with HIV. The working group has been convened to inform and develop 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: To date, the working group has defined peer, and peer health navigation; identified the guidelines' core values (GIPA/MIPA, harm reduction, anti-oppression, self-determination and resiliency); identified twelve core areas of practice to be covered in the guidelines; and established a participatory guideline development and review process. Once finished, the guidelines will go through an extensive community and expert review.

NEXT STEPS: The *Practice Guidelines in Peer Health Navigation for People Living with HIV* will be published in 2017.

EPHP15.02

Mobilizing Information, Preventing Infection: A Journey of Collaborative Knowledge Translation to Promote Youth-Oriented HIV/HCV Prevention in Nova Scotia

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Background: The three-year study "*Our Youth, Our Response*" (OYOR) examined youth-oriented HIV and Hepatitis C (HCV) prevention strategies in Atlantic Canada. The ultimate goal of OYOR was to provide policy and programming-relevant recommendations for improving youth-oriented prevention strategies across sectors in the province of Nova Scotia. To achieve this goal, the results of OYOR informed an iterative consultation titled *"Mobilizing Information, Preventing Infection,"* which involved an interdisciplinary team of stakeholders from across the province.

Methods: Knowledge translation and exchange (KTE) activities were completed to share best practice findings pertaining to HIV/HCV prevention across youth-related sectors. These activities included a one-day workshop, the production of topic-specific briefing notes and fact sheets, and a series of national webinars. The workshop focused on translating the key findings of OYOR into audience-appropriate KTE materials for policy decision makers, service providers, and community organizations. The webinar series was intended to stimulate interactive discussion and identify innovative opportunities for collaborative intersectoral initiatives focused on youth-oriented HIV and HCV prevention across Canada.

Findings: The key findings of OYOR consisted of five general strategies for improving youth-oriented HIV/HCV prevention across the four Atlantic Provinces. Although the consultation process narrowed its focus to reflect the Nova Scotian context, it allowed greater interprovincial/intersectoral recommendations for capacity building to transpire. General strategies for improving youth-oriented prevention were adapted to reflect the policy landscape, community context, and health infrastructure of Nova Scotia. Through stakeholder review, the presentation and wording of messages was refined to reflect knowledge preferences and needs of diverse policy and programming audiences.

Conclusion: This presentation will offer an overview of the process of adapting research findings to generate tailored dissemination materials for specific HIV/HCV prevention stakeholder audiences, and conclude with an overview of strategies identified for promoting collaborative production of HIV/HCV prevention-related KTE materials.

EPHP15.03

Responsive and integrated programming approaches for priority populations in hepatitis C

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CATIE, Toronto, ON

Background: Programs around the country are providing responsive hepatitis C services for priority populations across the continuum of care. In order to develop, replicate and scale up these effective programs, it is critical to identify the key factors of success at the programmatic, organizational, structural and systemic levels.

Purpose:

CATIE hosted a *National Deliberative Dialogue on Responsive Integrated Approaches to Hepatitis C Programming and Services* to explore front-line hepatitis C continuum of care models for priority populations (Aboriginal peoples, people who inject drugs, immigrants and new comers, HIV positive men who have sex with men, people in prison and older adults) and to identify promising directions in hepatitis C programming, policy and knowledge exchange.

Objectives: The deliberative dialogue had four primary objectives:

- inform priority directions for population-specific hepatitis C programming, services and policy that put service users at the centre of an integrated framework;
- provide guidance to new programs across Canada on hepatitis C continuum of care models for specific populations;
- facilitate multi-region, cross-sectorial collaboration, knowledge sharing and networking among hepatitis C programming leaders;
- inform a national strategic directions document.

Methods: CATIE organized a national knowledge exchange meeting on February 11-12, 2015. Select individuals were invited to attend with the aim of ensuring regional diversity as well as representation from the broader sector. Recommended factors of success in hepatitis C programming were extrapolated from the presentations and discussions at the Deliberative Dialogue.

Results: A total of 34 recommended factors of success were identified that foster integration and enable the development of responsive models of care which are accessible, relevant and effective at addressing hepatitis C.

Conclusions: In order to replicate, scale up and continue to improve the response to hepatitis C, the recommended factors identified at the Deliberative Dialogue may be critical to success.

EPHP15.04

Correlates of Hepatitis C Infection among Street-Involved Youth in Kingston, Ontario

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Background: Few studies have examined risk factors for hepatitis C infection among street-involved youth in Canada, and those that have focus on large cities such as Montreal, Toronto or Vancouver. Street-involved youth, who are of low SES status and often live in non-stable housing, have been shown to be at increased risk of contracting hepatitis C due to their increased likelihood of obtaining tattoos from unlicensed sources, sharing drug use supplies, and having unprotected sex with multiple partners. Whether and how these findings extend to smaller cities, however, is largely unknown. This study aimed to investigate which risk factors predict being positive for hepatitis C among street-involved youth in Kingston, Ontario.

Method: Self-report questionnaires were administered to a sample of 96 street involved aged 14-26 (53.1% female), who were recruited from several social service organizations that serve this population.

Results: Bivariate analyses showed that age (r=.25, p=0.02), having no high school diploma ($X^2_{(2)}$=7.26, p=0.03), and receiving tattoos from unlicensed sources ($X^2_{(2)}$=6.93, p=0.03), were significantly associated with being hepatitis C positive. In multiple logistic regression analyses, only age (B=0.36, OR=1.45, p=02), and having no high school diploma (B=2.694, OR=14.80, p=0.04) remained significant predictors.

Discussion: Known predictors of testing positive for hepatitis C from studies of street involved youth in large cities, including sharing drug supplies and having unprotected sex, were not found to be significant in this sample. Whether this is due to differences between youth in large versus smaller cities, or is due to aspects of our study design such as our reliance on self reporting and the small number of participants reporting being hepatitis C positive (n=8), will need to be confirmed with future work. Implications of this study for service providers include encouraging youth to obtain tattoos from licensed sources, and to complete their high school education.

EPHP15.05

CATIE Forum: Making it Work, From planning to practice

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Background: Our ability to improve the effectiveness of our HIV and hepatitis C (HCV) response has never been more certain. We are in time of global consensus that the knowledge and biomedical tools now exist to end HIV. At the same time, there is optimism about the changing landscape in HCV given the availability of better tolerated, more effective treatment. This knowledge has the potential to significantly transform our national frontline response, but uncertainty exists on how these developments will affect practice.

Methods: In October 2015, CATIE hosted its third national Forum with over 380 people, including HIV and HCV planners, service providers, researchers and policy makers, as well as people living with HIV and lived experience of HCV. The two-day agenda included 63 speakers in 23 sessions. Topics focused on each stage of the HIV and the HCV continuums, including new knowledge in research and programming and key population-specific implications of this knowledge. Objectives were to: encourage dialogue on programming implications of new HIV and HCV knowledge; examine evidence-based programming across the continuum; and encourage a population-based, syndemic approach to addressing HIV and HCV. The Forum was evaluated by CATIE via a form distributed at the end of the event.

Results: The Forum shared information pertinent to the changed world of HIV and HCV. 100.0% of participants agreed that the Forum was relevant to their work; 98% agreed that the Forum increased their knowledge of HIV and/or HCV programming; 95% agreed that the Forum increased their capacity to respond; 98.3% agreed that they will use/apply the knowledge gained.

Conclusions There is a desire nationally to engage in dialogue on programming implications of new HIV and HCV knowledge and examine evidence-based programming. National forums are effective venues to facilitate this engagement and CATIE is well positioned to curate such events.

EPHP15.06

Engaging Health Care Providers in Rural and Remote Settings through a Live Course on Community-Based and Culturally Relevant HIV Diagnosis and Treatment in BC and SK

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of Health Sciences, Burnaby, BC 15. University of British Columbia Hospital, Vancouver, BC 16. Canadian Aboriginal AIDS Network, Dartmouth, NS

Background: HIV disproportionately affects First Nation, Inuit and Métis Peoples (FN/I/M) and healthcare providers serving these communities often have limited knowledge of HIV diagnosis and treatment. In 2012, an online accredited course was launched to better inform healthcare providers about HIV as well as the cultural and historical frameworks in FN/I/M communities. In 2013, a live course was offered for BC and SK healthcare providers working in rural and remote communities.

Methods: Both courses had three main learning objectives: 1. Describe how to diagnose and treat people living with HIV and be aware of primary care guidelines; 2. Recognize social and physical barriers to care and describe supports available to persons living with HIV using an interprofessional model; and 3. Recognize the diversity of FN/I/M communities and integrate culturally appropriate and community-based healthcare models into practice. A combined quantitative and qualitative survey was given to attendees. Participants included physicians, community health nurses, nurse practitioners, community health representatives, and other healthcare providers.

Results: 284 healthcare providers in 14 communities participated in the live course between April 2013 and December 2015. The survey was given in 11 communities with a 56% response rate (131/232). A majority of respondents felt that the course was relevant (88%), provided valuable content and clinical information (92%), and met the course objectives (88%). The responses on topics for future programming indicate that the course needs to be tailored for local communities and adapted for community readiness.

Conclusions: The live course engaged healthcare providers by bringing them together to discuss culturally relevant HIV diagnosis and treatment in a community setting. Participants in BC and SK networked with HIV prevention and treatment experienced clinicians, respected community workers and Elders. Discussions included operational and implementation barriers to care, including scaling up HIV testing and referral pathways to care.

Social Sciences

Sciences sociales

Aboriginal Health
Santé des Autochtones

SSP1.01

Increasing HIV Testing on Reserve: The Village of Wellness Toolkit

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Background: In 2013, Vancouver Coastal Health (VCH) and Providence Health (PHC), working with an Indigenous consultant, conducted an analysis of existing HIV services in the 14 First Nations within the VCH region. This work highlighted that access to HIV prevention, testing and care varies greatly within the communities. VCH/PHC, in consultation with First Nations Community Health Directors and other stakeholders identified access to HIV testing as a key priority. The Health Directors of the 14 First Nations provided direction that any testing initiative would need to be holistic and incorporate a broader understanding of health and wellness.

Objective: Increase HIV testing on Reserve by adapting a holistic wellness fair model from Australia to better reflect the First Nations health context and support delivering the fair on reserve.

Methods: VCH/PHC Regional HIV Services and the Health directors formed a community-based working group that worked to adapt an existing tool to create the "Village of Wellness Toolkit": a guide for a holistic wellness fair which includes HIV testing amongst many other health screenings. This guide builds on wise practices from each community and reflects the First Nations cultures of the region.

Results: The Village of Wellness has been implemented in 4 First Nations communities. 2 of the four communities had not previously offered HIV testing in their communities. Between 10 – 20 individuals were tested at each fair. As yet, there have been no reactive HIV tests.

Discussion: Strengths of this model include strong community leadership and participation and increased reach of HIV testing in these communities. Limitations include a low yield of HIV positive tests. Once the Village has been implemented in all communities we will be able to better assess efficacy of this intervention.

SSP1.02

Engaging Community in Guiding Research Excellence National Aboriginal Research Advisory Committee

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Since 2006, The National Aboriginal Research Advisory Council (NARAC) has guided the research work of the Research and Policy Unit (RPU), and now the Aboriginal HIV and AIDS Community-Based Research Collaborative Centre (AHA Centre) at the Canadian Aboriginal AIDS Network (CAAN).

NARAC's mandate is to provide leadership, advice, support, vision and direction in all areas of research within CAAN and the AHA Centre. NARAC as an Aboriginal community ethics review board provides leadership, ensures that research is grounded in community and is grounded in Aboriginal culture. Council members are engaged based on past and continued involvement in the Aboriginal and/or the Community-based Research community, for all of CAAN's and the AHA Centre's research initiatives. NARAC works to ensure that CAAN undertakes and produces HIV and AIDS research that is methodologically-sound, culturally-appropriate, respectful, and relevant. NARAC also ensures that CAAN and the AHA Centre comply with the guidelines set out by the TCPS2 –Chp. 9.

The development of a CAAN advisory Council requires consideration for diverse representation, perspectives and experience. Key considerations include inviting First Nations, Inuit and Métis peoples and Aboriginal people living with HIV (APHAS). Attention must also be given to representation from across Canada, roles with community-based organizations and academic institutions, age, gender and cultural protocol such as Elder guidance.

This presentation will highlight NARAC's work guiding CAAN to do community-based research in a "Good Way". This presentation will explore what it means "do to research in a good way" and the value of an Aboriginal community research ethics board such as the role NARAC plays in ensuring this has been done. We will discuss our successes in engaging the Council in research, as well as some of the challenges we have faced and lessons learned (or in progress) to overcome them.

SSP1.03

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 not unrealistic to think that HIV rates in Inuit communities could rise dramatically if no action is taken to scale up prevention efforts. 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.

SSP1.04

Positive Aging: Indigenous peoples aging with HIV/AIDS

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As a result of advances in treatment over the past 30 years, the number of older people living with HIV is growing. This is of particular concern for Indigenous populations in Canada given continuing over representation in HIV diagnoses. While there has been an increase in research on aging with HIV within the general population, little is known about the experiences of older positive Indigenous peoples.

Research was conducted in partnership with the Canadian Aboriginal AIDS Network (CAAN) at CAAN's Wise Practices V conference. Participants were conference delegates, representing a sample of First Nations, Inuit and Métis people living with HIV and/or service providers from across Canada. Participants ranged in age from 32 to 63 and had been positive for 5 to 29 years. Data was collected through four sharing circles (two with women, one with men and one with service providers) and four interviews (n=34).

An open analytic approach was used to explore the content of the transcripts and codes were collaboratively developed by the research team through an inductive and iterative process. Our preliminary findings reveal several dimensions which facilitate successful aging (SA) within this population: physical, emotional, spiritual, mental and social health. While the dimensions which an individual must embrace in order to achieve SA are intricately connected, the emphasis that one places on each dimension is subjectively determined. Participants recognized the interconnectedness of the dimensions and the importance of finding the right balance between each dimension in order to actualize SA.

The goal of this project was to identify facilitators and individual strategies which enable SA within this population, in order to develop culturally mediated responses. Ideally, this knowledge can be used to help structure community and primary health services to promote SA with HIV in ways which are congruent with Indigenous culturally-defined notions of health.

SSP1.05

The Cedar Project: Culture and language support resilience among young Indigenous women involved in sex work in Vancouver and Prince George, BC

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Background: Indigenous leaders have long argued for acknowledging the role of culture, familial relationships, and community as integral to understanding resilience among those involved in sex work.To our knowledge, no previous epidemiological studies have explored the effects of historical and lifetime trauma, cultural connectedness and risk factors on resilience for young Indigenous women involved in sex work.

Methods: The Cedar Project is an ongoing prospective cohort study of young Indigenous people who use illicit drugs in Vancouver & Prince George, BC. This study explored protective and risk factors associated with resilience among young Indigenous women who use illicit drugs and reported ever being involved in sex work. We utilized the 25-item Connor-Davidson Resilience Questionnaire (CD-RISC) to measure resilience and data on drug use and sexual risk between 2011 and 2014. Linear mixed effects models estimated the effects of the study variables on mean change in resilience scores.

Results: Among 161 participants, 47% had a parent who attended residential school, and 73% had been in foster care. HIV(B=-0.98, p=0.782) and HCV (B=4.863, p=0.121) positive status were not significant in unadjusted analysis. The overall mean resilience score was 61.58. Adjusted factors associated with higher mean resilience scores included living by traditional culture (B=6.218, p=0.005), knowing how to speak a traditional language (B=4.020, p=0.025), having grown up in a family that often/always lived by traditional culture (B=5.109, p=0.012), and having recently had counselling (B=3.331, p=0.050). Adjusted factors associated with diminished mean resilience scores included injection drug use in past six months (B=-3.828, p=0.055).

Conclusion: Despite facing alarming levels of intergenerational and lifetime trauma including drug and sexual related vulnerabilities, cultural connectedness is associated with higher resilience among young Indigenous women involved in sex work.

Combining Prevention Strategies: Social Scientific Perspectives
Combinaison des stratégies de prévention : perspectives des sciences sociales

SSP2.01

Latino MSM at risk for HIV/STI's on Online Apps, in Toronto, Canada: The Urgent Need for Online Outreach services, a PROGRAM SCIENCE approach

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Summary: In a population scan of Latino MSM individuals at high risk of HIV/STIs, a data request to GRINDR (the popular sexual network online app) was issued. A number of 1,980 (January, 2015) and 2,670 (September, 2015), self-identified Latino MSM were found (ONLY) in the city of Toronto.

Issues: The *Program Science* approach recommends the use of attainable, community achievable/evidence based strategies for effectively intervening in the community's positive sexual health outcomes. Funding issues in Toronto, Ontario are affecting the likelihood of Latino MSM individuals increasing their health literacy, self-agency and sexual health decision-making.

Description: Lack of epidemiological numbers that are both: scientifically statistical valid, and representative of sexual health at risk individuals are hard to obtain. This factor gets worse when working with vulnerable minority groups. Nonetheless, The OHTN has released a study (1) Choi et al., (2015) where an economic evaluation on HIV prevention programs was conducted revealing positive outcomes for taxpayers.

Analysis Results:

- HIV community prevention programs are considered successful from an economic perspective; taxpayers receive back approximate $5.00 dollars, for every dollar invested.
- According to the OHTN rapid response document, it has become necessary the conduction of Online HIV/STI's Outreach prevention efforts.
- Other agencies in Canada have already established Online Outreach activities that could be easily adopted by marginalized community groups.

Lessons Learned:

- To provide funding for Outreach Online programs for Latino MSM in Toronto, Ontario, Canada, make sense from myriad approaches: economic criteria, as means of intervening in individuals' sexual health literacy, and from a program science/evidence-based perspectives.

1. Choi, S. K. Y., Holtgrave, D. R., Bacon, J., Kennedy, R., Lush, J., McGee, F., Tomlinson, G. A., Rourke, S. B. (2015). Economic Evaluation of Community-Based HIV Prevention Programs in Ontario: Evidence of Effectiveness in Reducing HIV Infections and Health Care Costs. *AIDS and Behavior*. doi: http://doi.org/10.1007/s10461-015-1109-8

SSP2.02

JD and the Sunshine Band: The Continuing Story of Recreation as HIV Prevention

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Background: In 2012, *Sunshine House*, a community-based organization that works with underserved populations, developed the *Solvent Users' Recreation Project* (SURP). SURP involved eight interactive modules, each for 5 – 8 weeks, including activities such as boxing, art, automotive repair, and creating and performing music. The success of SURP provided the creative energy for the evolution of *JD and The Sunshine Band*; this band showcases the talents and collaboration of program participants, professional musicians and Sunshine House staff. The momentum of *JD and the Sunshine Band* supports the idea that recreation programs can be a form of HIV Prevention.

Objectives: Through participation in *JD and the Sunshine Band*, "The Shiners" (participants) fully engage in collaborative creative expression, broaden their circles of social support, explore forms of literacy, and identify as "rock stars". An important outcome of participation is that individuals who are often passive recipients of resources become active contributors through sharing their music.

Methods: Participation in *JD and the Sunshine Band* is multifaceted and has involved participants collaborating to write song lyrics, assisting with musical arrangements, attending band practices, recording a full length album, creating cover art and liner notes, planning and performing a sold out cd release show, conducting media interviews, and actively playing concerts in Winnipeg and the surrounding area.

Results: It has been suggested that people who use solvents are unable to access recreational services because of the unstable nature of their lives. However, *JD and the Sunshine Band* demonstrates that people who use solvents can benefit from recreation services when programs are available and participant-driven.

Conclusions: Engaging in recreational activities such as this suggests widespread benefits for physical and mental health. Specific to HIV prevention, this initiative facilitates access to harm reduction supplies, broader social networks, and opportunities for organic HIV information sharing.

SSP2.03

Sexual Health Assessment (SHA) Training: Increasing Provider Capacity Around HIV/STBBI Testing and Incorporating Best Practices Into Routine Health Care

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Introduction: Barriers to HIV/STBBI testing include: client discomfort, stigma, service provider lack of knowledge around risk factors and testing options, time constraints during appointments, and assumptions about client's 'safe' sexual activity (or inactivity). It is important in HIV prevention to normalize HIV/STBBI testing as a routine and essential component of overall care.

Background: Nine Circles' SHA is a unique training for clinicians that provides capacity-building and practical clinical skills (assessment, specimens, when to test (window periods)), as well as broader variables key to comprehensive sexual health assessment, testing, and treatment, such as sex positive language, cultural sensitivity, available resources, acknowledging provider biases, and approaches to harm reduction.

Methods: Using pre and post-training self-assessments, participants were asked to rate their level of competency in several aspects of knowledge and skills prior to, and upon completion of the training, and identify new strategies they intend to incorporate into their practice.

Results: The outcomes include self-reported increase in: knowledge of HIV/STBBI, competency in the aspects of testing, and knowledge of culturally appropriate and sex positive approaches. On average, 95% of participants (n = 12) indicated they feel competent across the ten areas of training, as compared to 52% indicating they feel competent prior to the training. The majority of participants (91%) indicated intent to adjust service delivery; among the strategies: adding new questions to sexual health history taking, obtaining specimens in addition to urine collection (swabs), adjusting the language they use during visits, and encouraging colleagues to conduct more testing. Additional results will be presented (training is scheduled for February, 2016).

Conclusions: Participants are better able to foster safe spaces for a dialogue around sexual health, testing, and follow-up. Further trainings are planned as we work to reduce stigma around HIV/STBBI within health care settings, and increase provider capacity to test.

Critical Approaches to Community-Based Research
Approches critiques à la recherché communautaire

SSP3.01

Advancing Scoping Study Methodology in the HIV Community: Perceptions on Methodological Steps and Ways to Enhance Scoping Studies in HIV Community-Based Research

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Objectives: Scoping studies (or reviews) are an increasingly popular form of knowledge synthesis in the field of HIV research that involves mapping the evidence in an emerging field to inform and justify future research, practice, programming, and policy. Our aim was to understand the experiences of, and considerations for conducting scoping studies from the perspective of academic and community partners. We specifically describe considerations for enhancing scoping study methodology in the field of HIV using a community-based approach.

Methods: We conducted a cross-sectional web-based survey with researchers, community members, representatives from community-based organizations (CBOs), and policy stakeholders with experience and/or interest in scoping studies to gain an understanding of experiences and perspectives on conducting scoping studies. We administered an electronic self-reported questionnaire comprised of 22 items related to experiences with scoping studies, strengths and challenges, opinions on terminology, and methodological steps. We analyzed questionnaire data using descriptive statistics and content analytical techniques. Survey results were discussed during a multi-stakeholder consultation to identify key considerations in the conduct and reporting of scoping studies.

Results: Of the 83 invitations, 54 individuals (65%) completed the scoping questionnaire, and 48 (58%) attended the scoping study meeting from Canada, the United Kingdom and United States, including community members and representatives from CBOs. Many scoping study strengths were dually identified as challenges including breadth of scope, and the iterative process. We offer considerations for CBOs on how scoping study methodology can augment their research capacity. We explore how this methodology, combined with the experiences of CBOs and a HIV community-based research approach, can enhance consultation, integrated knowledge translation, and interdisciplinary team based research.

Conclusions: Scoping reviews have potential to advance HIV care, programs and policy. Better understanding ways in which community-based research may enhance the

conduct and reporting of scoping studies will help achieve this potential.

SSP3.03

HAND MAPPING (HaM) is a 'scaled down' Body Mapping (BM) Evaluation Qualitative Method: Understanding Gay Sexual Health Practices and HIV/STI's Life Trajectories

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Summary:

Topics related to useful qualitative evaluation methods are commonplace when trying to depict sexual health practice narratives, particularly among strategies that pay attention to life trajectories. *BM* are research methods that have helped to understand the experiences of undocumented migrants in Canada. At the same time, *BM* requires resources, e.g. space, money, time; that are not always available for community organizations.

Issues:

New visual descriptive-methods for program evaluation are needed in order to represent better the life experiences of marginalized individuals. Particularly when representing sexual health practices that are related to experiences and major lived events, such as: being born in another country, "coming out", first gay experience, migration, being diagnosed as HIV+, PrEP, etc.

Description:

HaM use, same as *BM*, the body (hand) configuration drawn on a piece of paper. Participants use their own hands to represent the five fingers and the hand's palmlines, representing participant's major life events and experiences as well as their sexual health practices. Stories about love, passion, sexual orientation, migration and HIV/STI's are easily elicited. An autobiographic-narrative or a semi-structured interview may be used to complement the inquiry.

Lessons Learned:

- *HaM* has the potential of becoming a useful qualitative visual narrative-method for community organizations. Due in particular to the method being simple, accessible and easy to apply.
- *HaM* has the quality of allowing community organizations to visually see and understand individuals' needs, learning outcomes, deficits and shortcomings. At the same time, it is an excellent prop to elicit conversations and focus-group discussions if shared with other participants.
- The limitations and ethical considerations are very common to visual participatory methods. Therefore, same policies and protocols should be set in place.
- *HaM* has the potential of depicting those particular narratives, using visual props, and helping to communicate ideas to policy makers, researchers and interventions.

SSP3.04

PrEP arandote (Getting Ready): Theoretical Approaches for the Future Use of New HIV Prevention Technologies, Access Issues among Spanish-Speaking MSM in Canada

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Summary: PrEP (Preexposure Prophylaxis) is a pharmaceutical tool that is known for reducing the risk of HIV infection. In Canada, PrEP has been supported by some relevant health institutions as a possible tool for reducing the risk of MSM (it is suggested that condoms be used along with PrEP).

Issues: PrEP has become available more than 30 years after the beginning of the HIV epidemic in Canada. New evolving discourses in HIV have changed rapidly as new pharmaceutical-tools are introduced in the social-milieu. Basic questions include: Who will have access to PrEP? Who is going to pay for it? What is the future role of HIV prevention as we know it? How do migrants/vulnerable-marginalized individuals get access to newer-safer-sex-options in Canada?

Discussion: Spanish-speaking-MSM in Canada are formed mostly from immigrants. MSM-individuals face great challenges in Canada. Immigration issues, homophobia-rejection, are still issues faced by this group. Many of those MSM struggle with problems related to their own sexual-desires, and identities-social needs. PrEP offers a new window for SPP-MSM to reconcile their sexual-practices with their own HIV-prevention-objectives. As the current field evolves, PrEP has not reached the level of becoming a "free-access" medication. Accessibility issues are to be called for analysis.

Discussion:

- Community discussions about people using PrEP and being called "whores" is still a common place. Stigma, ignorance and lack of health literacy are to be acknowledged.
- Access to PrEP as a tool for prevention is quetionned in Canada, since, it is up to the individual and his own means (private insurance) to have access to this prevention tool.
- The medical field in Canada, needs to acknoledge the sexual desires, pleasures and passions of SPP-MSM.
- Social Determinants of Health in migrants, racialized and sexual minorities require a deeper analysis and better policies, if aiming for an effective HIV reduction.

SSP3.05

Using community mapping in a participatory consultation about PHA needs from an ASO: the Peel Region HIV/AIDS Network experience

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Overview: From 2014 to 2015, the Peel HIV/AIDS Network (PHAN) conducted a peer-led consultation to identify the needs of people living with HIV (PHAs) in the region and to encourage the greater and more meaningful involvement of people living with HIV.

Methods: Five peer consultants formed a team and were trained using the OHTN's Universities Without Walls eLearning modules. *Community asset mapping* as set out by Kretzmann & McKnight (1993) was adapted to the context. The training sessions taught the basics of: qualitative interviewing, focus group facilitation and community mapping; safeguarding confidentiality; and analyzing visual and written information.

The community consultation took place between February & May of 2015. Participants were recruited through e-lists, newsletters and a video. The three highly social mapping sessions lasted up to three hours. Prompted by scripted questions, participants freely drew symbols on and added text to large pieces of paper (the maps). One peer consultant facilitated each session and another served as note taker.

Results: Results showed the disadvantages PHAs face in Peel and the role PHAN plays in outreach. For example, we learned that PHAs try to avoid stigma by seeking services in Toronto and by not disclosing their HIV status to all service providers, family members and/or caregivers. Paradoxically, attempts by PHAs to hide their HIV status tend to make PHAN less visible in the region.

Key Recommendations: PHAN now plans to: connect to informal supports that make a difference to PHAs (such as faith-based organizations); enhance its role in helping PHAs gain access to medication; enhance its online presence; and develop a stronger relationship with HIV-related services in Toronto to have them refer PHAs back to PHAN. The GIPA-strong methods and process can be adapted to the needs assessment and strategic planning similar semi-urban organizations.

SSP3.06

Developing evidence informed interventions to promote resilience amongst Asian MSMs across life challenges- the MSM Resilience Dialogues

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Background: Asian men who have sex with men (MSM) in Canada face complex challenges related to the compounding impact of racism, homophobia and HIV stigma. To develop evidence-informed strength-focused programming, Asian Community AIDS Services (ACAS) in Toronto conducted the Asian MSM Pathways to Resiliency (AMP2R) community based research study.

Methods: AMP2R engaged 51 Asian MSM and 12 service providers to explore the factors, pathways and strategies that Asian MSM used to access protective social determinants, and to navigate through major life transitions. Participants identified coming out, migration, encountering HIV and navigating sex and relationships as critical life transitions that impact their sexual health. Cross-cutting resilience strategies identified included: balancing enculturation and acculturation to foster positive identity; planned migration from oppressive environments; creating alternative support networks; commitment to self-care; and accessing culturally safe programs/services.

To develop evidence informed interventions based on CBR principles, the research team created meaningful community campus partnerships to conduct literature search, program scanning and stakeholder consultation to capture frontline knowledge and lived experiences on potential interventions that will support skill development in the identified cross cutting resilience strategies. Research team members then synthesized core intervention components to develop an original intervention called the MSM Resilience Dialogues (MSMRD).

Results: The MSMRD intervention consists of 5 sessions and aims to promote resilience through dialogue, critical self and group reflection, value clarification and experiential learning. 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.

Conclusion: The meaningful community engagement in the developmental process of the intervention ensured its relevance and stakeholder buy-in. The intervention has been piloted through the various programs in ACAS with promising results and is being planned for cross cultural adaptations across other racialized MSM communities in Toronto.

SSP3.08

The BC People Living with HIV Stigma Index Project: Planning Phase Evaluation

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Background: The People Living with HIV (PLHIV) Stigma Index is an international tool aimed at identifying the intersections of society where HIV stigma persists. It has been conducted in over 50 countries and British Columbia will be the pilot region for the Canadian implementation of this community-based research (CBR) study. We conducted a process evaluation to assess whether the planning phase has proceeded in a manner adherent to CBR principles.

Methods: All BC planning phase team members, including 6 PLHIV, 2 service providers and 2 researchers, were invited to participate in the evaluation. Three methods of data collection were used – online survey (n=8), interviews (n=2), and participant observation. The survey and interview asked respondents about the project's respect for CBR principles, reflections on and impacts of their involvement, and recommendations for the national implementation.

Results: Overall, respondents indicated satisfaction with the project, particularly its necessity; this echoes other studies and reports that highlight stigma as a pressing issue in the lives of PLHIV. With respect to team engagement in study activities and decision-making, respondents indicated that they felt they were actively engaged in most areas, and indicated areas for increased involvement and capacity-building. One challenge identified for the planning phase was team diversity and the ability to engage team members from more rural and remote areas of the province. While many attempts were made to diversify the team, this continued to be a challenge due to geographic and community capacity limitations. Overall, team members found this CBR process valuable and necessary for addressing HIV stigma in BC.

Conclusion: Overall, the planning process for the BC Stigma Index has shown genuine respect for CBR principles. Considerations for implementation nationally and for the next phase in BC include enhancing efforts to diversify the team, continuing to prioritize capacity-building, and ongoing evaluation.

Critical Social Theory: Applications and Advancements in Understanding the HIV Epidemic
Théorie sociale : Applications et progrès dans la compréhension de l'épidémie de VIH

SSP4.01

Health Care Access Among Older HIV-Positive LGBTQ Adults: Conceptualizing the Field for Empirical Inquiry

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Older lesbian, gay, bisexual, transgender, and queer (LGBTQ) adults living with HIV continue to experience systemically inequitable access to health care services, often based on factors ranging from HIV stigma to homophobia and gender-based violence. Accordingly, the pursuit of theoretical and empirical inquiry on phenomena of health care accessibility among this population is arguably relevant and necessary. Despite the growing relevance of engaging in this field of study, however, there remains a relative dearth of theoretical works that explicitly consider and address the social conditions of health care access among older LGBTQ adults with HIV. This poster summarizes the contents of a paper whose purpose was to conceptualize issues of health care access in aging sexual and gender minorities who are HIV-positive, particularly with reliance on the theoretical traditions of Foucauldian governmentality and intersectionality to frame and analyze the limited body of relevant empirical literature. Whereas the former framework was employed in this paper to draw attention to phenomena of surveillance and control that characterize health care access among older HIV-positive LGBTQ adults, intersectionality was used to highlight potential idiosyncrasies in these problematic experiences of accessing care across this population, many of which reflect the complex and multifaceted configurations of social location among LGBTQ elders with HIV. The poster emphasizes implications of the paper's analysis on research and policy, specifically by outlining theoretically congruent programs of research that may promise to generate an evidence base for informing policies associated with enhanced access to care among older HIV-positive LGBTQ adults. Additionally, examples of policy initiatives that are likely to emerge from this empirical knowledge base, and that are in turn likely to improve health care access among this underserved population, are tentatively considered.

SSP4.02

"Sexual Health Messaging Trajectories:" Turning HIV Risk on its Head

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This presentation will focus on how African newcomer teen girls and young women come across and interpret sexual health messaging in their everyday lives, and in particular messages relating to HIV. These findings are based on ethnographic community-based research conducted in Winnipeg during 2014 and 2015, where I worked with peer researchers from African communities as well as with local organizations that provide support for immigrants and refugees. More specifically, I explore how a research instrument called "sexual health messaging trajectories" has garnered insights into how HIV vulnerability (or "risk") and prevention are understood, negotiated, and resisted by an at-risk population within a Canadian context. What was striking was how most of the 10 participants expressed their experience of seeing fewer HIV-related sexual health messages in Canada compared to their experiences in various African countries. The power of these messages and the communication of vulnerability to HIV, among other consequences, through sexual contact were contradictory. Within the sphere of public health, particular groups including youth, women, and newcomers from HIV-endemic countries, have been singled out as "at-risk" for contacting HIV. However, in analyzing the sexual health messaging trajectories of African newcomer girls and women living in Winnipeg, it was understood that everyone who engaged in sexual activity was vulnerable. Therefore, Canadian born youth were more "at-risk" than African youth, in their eyes. The friction between the ways in which HIV risk is broadly conceptualized and how participants took up and re-shaped these discourses offers insights into how these categorizations operate at the everyday level of experience. This, is turn, opens up a productive space for analyzing the complex aspects of seemingly neutral public health messages

Engaging (with) Communities in HIV Research Participation des collectivités à la recherche sur le VIH

SSP5.01

"In Real Life": Social, Communal, and Attitudinal Covariates of Online Sex-Seeking (OSS) among Gay, Bisexual, and other Men who have sex with men (GBM) in Vancouver

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Background: Online Sex Seeking GBM have been described as "disconnected" from the gay community and "at risk" for HIV. However, little research has actually focused on the social and attitudinal factors associated with OSS.

Methods: We used Respondent-driven sampling to recruit sexually-active GBM, aged ≥16 across Metro Vancouver from 02/2012-02/2014. Participants self-completed a computer-administered questionnaire reporting their demographics, levels of Social Support, Communal Sexual Altruism, Loneliness, Collective Self-esteem, participation in gay sports, gay-specific groups, gay bars/clubs, pride events, gay media consumption, GBM network size, time spent with GBM, and other sexual/prevention-related behaviors. A multivariable logistic regression model for any sex-seeking using mobile apps/websites in the past six months was created using backwards selection AIC minimization.

Results: Of 774 participants, 68.8% were white, 79.9% gay-identified, and 78.6% HIV-negative with a median age of 34 years. In multivariable results, OSS (reported by 67.3% of participants) was less likely among GBM who were Aboriginal (OR=0.43, 95%CI[0.23,0.82]), or spent little social time with other GBM (OR=0.45, 95%CI[0.30,0.69]); and more likely among those reporting: ever getting an HIV test (OR=4.35, 95%CI[2.12,8.93]), more Facebook friends (OR=2.88, 95%CI[1.40,5.94]), being single (OR=2,81 95%CI[1.91,4.12]), recent condomless anal sex with a serodiscordant/unknown partner (OR=2.39 95%CI[1.51,3.79]), always asking their partner's status (vs. never/rarely/sometimes, OR=2.12, 95%CI[1.29,3.50]), greater Sexual Sensation Seeking (OR=1.06, 95%CI[1.01,1.11]), greater Anxiety (OR=1.05, 95%CI[1.00,1.10]), younger age (OR=1.04, 95%CI[1.02,1.06]), more male anal sex partners (OR=1.02, 95%CI[1.00,1.05]), lower Collective Self-Esteem (OR=0.91, 95%CI[0.85,0.99]), and lower Communal Sexual Altruism (OR=0.71, 95%CI[0.53,0.95]).

Conclusion: OSS-GBM were more likely to be younger and single, and less likely to identify with the gay community. This is, despite their spending a significant amount of social time with other GBM, having more Facebook friends,

and more anal sex partners. This suggests OSS may be part of a distinct pattern of gay sociality occurring within personal/sexual networks rather than traditional/institutional parameters.

SSP5.02

Yes We Can! Ensuring Momentum, Motivation and Morale in a long term Community Based Research Project: The Canadian HIV Women's Sexual and Reproductive Health Survey

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Introduction: As a national, community-based cohort study, CHIWOS is committed to the "Meaningful Involvement of Women Living with HIV (MIWA)". Since launching the survey phase in October 2013, the research team experienced a variety of challenges including transitions in staff and peer research associates (PRAs) (women with HIV with research training), maintaining momentum into the 18-month follow-up visit (Wave 2), reconnecting with participants many who are harder-to -reach. There is also a concern about ongoing support for the PRAs.

Methods: A national team of CHIWOS PRAs academics, and community researchers examined the question using a MIWA framework: How do we maintain momentum, motivation and morale over time in a long-term project and ensure the integrity of the project's guiding principles is met?

Results: Reflecting on differences between recruiting and reconnecting existing participants as well as bureaucratic challenges in moving projects ahead which can sometimes be time consuming, the team found additional challenges during the uptake of the second wave of the CHIWOS questionnaire. The introduction of new staff and PRAs resulted in group dynamic changes, needs and expectations. The ongoing study momentum and support required a variety of responses. In-person training and ongoing monthly PRA teleconferences were essential. A PRA-buddy system was streamlined; women were encouraged to connect with others they connected well with. Self-care needs were essential to prioritize. The fact that loss-to-follow up and decreases motivation are natural occurrences in longitudinal studies was important to highlight and not indicators of success or failure.

Conclusions: Various challenges have occurred during the course of CHIWOS and were dealt with through MIWA approach. It is essential to address issues in a timely fashion to keep up morale and integrity in order to move forward in a way that achieves the original goals of the project and its guiding principles.

SSP5.03

HIV, Social Work, and Brain Health: A Mixed-methods Community-based Research Study

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It is estimated that 50% of people living with HIV in Canada will be affected by at least an asymptomatic form of HIV-Associated Neurocognitive Disorder (HAND) (St. Michael's Hospital, 2014). As the number of people living with HIV over the age of fifty increases, social workers and other helping professionals need to adapt to meet people's changing needs.

Using a Participatory Action Research (PAR) framework, a research team comprised of social workers and people living with HIV developed a mixed-methods exploratory study to understand the support service needs of people over the age of fifty who are living with HIV and concerned about HAND.

Through a survey and follow-up in-depth interviews with 20 survey participants, the research team set out to determine: a) the concerns that older adults living with HIV have about cognitive health; b) their knowledge and experience of social work; and c) what gaps they identify in current HIV-related programs and services related to cognitive health. The survey yielded 108 participants, of whom 88% identified as male, 66% were aged 50-59, and 54% were diagnosed with HIV before the introduction of Highly Active Antiretroviral Therapy (HAART) in 1996. For the interviewees, 25% identified as female.

An iterative data analysis process was employed whereby three independent coders used NVivo to separately identify key themes from the interviews. The peer researchers were presented with the three independent analyses and the research team collaboratively determined the project's findings. The findings speak to the existing reality of HIV-related support services and how to mitigate service barriers while enhancing client impact and engagement. These findings have important implications for the shape and content of programs and services for people aging with HIV, as we work towards improved health outcomes for people living with and affected by HIV/AIDS.

SSP5.04

Peer Researcher Support Project: Developing Support Tools for People Living with HIV Working in HIV Research

Terry Howard

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Developing Industry Support Standards for Peer Workers Living with HIV

Background and Rationale:

Employing peer workers as research associates, counsellors, clinic-based HIV service/support navigators and a variety of other employment opportunities is gaining popularity today as CBOs and researchers attempt to integrate GIPA/MEPA principles more comprehensively into new projects. The HIV community has responded by developing industry support standards for employing workers with HIV to adequately provide support based on the unique needs of this group of workers. Often unskilled in the conventional sense of their job descriptions, workers bring accessibility to the community, rich relationship opportunities and subject relevance, and personal history to their work. Specific supports are required to address the emotional, physical, financial, and personal intensity impact this employment has on these workers. By developing industry standards for support provision that can be adapted to various forms of peer employment, and openly discussing the needs of peer workers and including their input, we created and developed a valuable resource for researchers, CBOs, Health Authorities, and others who seek to employ people living with HIV.

Success and Next Steps: We conducted a series of Focus Groups with the community to gather data to develop support standards for peer workers living with HIV. Researchers, CBO staff, Health Authorities and peer workers were asked what types of supports are needed for peers working as research associates, counsellors, "navigators" and other employment. The research team presented existing examples of suggested conventional support services and asked participants to evaluate their effectiveness, and how to address gaps in current support tools in order to develop industry standards. From this work, a living document was created to provide support tool options known to be effective, and offer the opportunity for ongoing input into the resource as new support tools become known and utilized.

SSP5.05

PRA-plus: Building a Mentorship Program for Peer Research Associates Working in HIV Research

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The **PRA-plus** project is a mentoring program for Peer Research Associates (PRAs) to develop skills, knowledge, and support systems that expand opportunities for meaningful engagement in HIV/AIDS research.

We designed a pilot training program to support PRAs through the transition to 'PRA-plus.' Within a community-based approach to HIV research (CBR), people living with HIV are recruited, hired and trained to administer quantitative surveys. It is understood that this data collection is relatively entry-level work. Consequently, when PRAs become familiar with the entire research process, curiosity arises about other aspects. Seasoned PRAs who have been involved in CBR for a number of years now want to move on to the next level. We engaged community partners and PRAs to conceptualize how we could support PRAs to get there.

PRA-plus came from stakeholder discussions. We provide comprehensive support and training for PRAs to act as a role model to peers in PRA work, serve as leaders, and opportunities for personal and professional development. Transitioning PRAs to the role of PRA-plus equips individuals with additional skills and training beyond survey administration. PRAs are trained in high-level communication skills to go beyond listening, and to identify and conduct basic conflict resolution. In addition to practical self-care, they learn to identify when PRA peers are in need of self-care and help encourage this.

The success of PRA-plus provides the double benefit of utilizing new skills and providing advancement opportunities. Recent advances in HIV CBR are due in large part to the enormous contributions of PRAs. The time has come for reciprocity and a commitment to advancing PRAs beyond work that serves only the purposes of the project. It is our responsibility as researchers to provide them with the tools for success, to cultivate their strengths and to help guide them to the next level.

SSP5.06

HEADS UP! Using a modified DEPICT model for participatory analysis in a qualitative study of neurocognitive difficulties among people living with HIV

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Background: Despite the high prevalence of HIV-associated neurocognitive disorder (HAND), limited information exists about how people with HAND view, cope with, and speak about cognitive impairments. HEADS UP! used a team-based participatory analysis approach to explore the lived-experience of HAND at Casey House and St. Michael's Hospital (Toronto, ON) and The Dr. Peter Centre (Vancou-

ver, BC). Our interdisciplinary team included five Peer Research Associates (PRAs), four clinicians, four academics, and two students. PRAs received approximately 20 hours of training using a blended-learning strategy.

Analysis & Interpretation: Twenty-five adults recently diagnosed with HAND were interviewed by the Research Coordinator and Principal Investigator. Using Nixon & Flicker's DEPICT model for participatory qualitative analysis, interviews were transcribed verbatim and processed as follows: the first available set of 10 transcripts was coded by one academic and one PRA. In a day-long meeting with the research team (including only Vancouver PRAs to avoid *deductive disclosure*) following a *grounded theorizing* approach, we generated 25 descriptive codes and subsequently distilled these into 10 primary codes with 25 secondary codes. For example, the primary code "Actions taken over time to deal with HAND" was separated into secondary codes of immediate tactics (e.g., "laughing it off") and medium/long-term strategies (e.g., sticking to helpful habits and avoiding potentially embarrassing situations). The aggregation of each code was summarized and used to guide two additional full-team analysis and interpretation meetings.

Lessons Learned: Integrating PRAs' storytelling into the analysis and interpretation meetings is crucial to grounded theorizing and triangulation with existing clinical literature on HIV and HAND and to achieving *descriptive and interpretive validity*. The DEPICT model helps balance clinical/academic authority with the patient's common sense and eagerness for action. PRAs are crucial to a grounded knowledge to action process, and helped to build content for a webpage, video, and brochure about HAND.

SSP5.07

HEADS UP! Results of a qualitative study of the lived experience of HIV-associated neurocognitive disorder

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Background: Little is known about how individuals with HIV-associated neurocognitive disorder (HAND) view, cope with, and manage changes in memory, attention and thinking. HEADS UP! is a qualitative study exploring the experience of HAND among those who receive HIV care and support services at Casey House, St. Michael's Hospital (Toronto) and The Dr. Peter Centre (Vancouver). The goal of this study was to explore the trajectory and consequences of HAND and coping strategies.

Methods: Twenty-five adults were screened for HAND and debriefed by a clinician before participating in a 1.5-hour semi-structured interview. Questions prepared by study investigators and trained peer researchers focused on: (1) the trajectory of HAND; (2) HAND's effects on self-confidence, mood and resilience; and (3) the role of HAND in interactions with friends, family and healthcare providers. Transcribed interviews were coded and summarized by teams of at least two, including peer researchers.

Results: Participants reported HAND-related *adaptive* strategies (e.g., memory-aid support from friends and healthcare providers) and *maladaptive* strategies (e.g., long-term use of substances). Participants described experiencing increased confusion, anxiety and frustration; fear of losing one's identity; and living with the stigma of cognitive difficulty. They also described significant tactics in the moment, such as "laughing it off" (using humour to cover/dismiss symptoms). Consequences of HAND included material losses (e.g., misplaced cheques), missed appointments, and ART dosage errors. Participants' greatest supports were healthcare providers and intimate partners and yet they have few conversations about memory, attention and thinking.

Discussion: These descriptive results enrich our understanding of HAND as presented in the clinical literature. Examples of tactics and strategies can be used by people living with HIV or health care providers to start conversations about HAND. Key messages about living with HAND should be tailored to specific audiences, including tips for healthcare providers and people living with HIV.

SSP5.08

Developing and Evaluating a Patient Engagement Intervention in the I-Score Study: Involving HIV Patients in the Improvement of Treatment Adherence

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Introduction: Many HIV patients on antiretroviral treatment (ART) have trouble taking it as prescribed. These difficulties are insufficiently discussed in clinical encounters. The I-Score Study (CTN283) will develop a digital tablet-administered patient-reported outcome (PRO) to be integrated in clinical practice on patient-identified factors that interfere with taking ART. However, implementing PROs into care is met with mixed impacts on patient outcomes. Improving the success of PROs may depend on engaging patients in their development, but patient engagement interventions are rarely evaluated.

Objective: To describe the characteristics and evaluation design of the Patient Engagement intervention that complements the I-Score Study.

Method: The intervention includes a Montreal-based Patient Advisory Committee that meets regularly to discuss the ongoing developments of the I-Score Study. The

evaluation's design consists of an ethnography based on a participatory approach.

Results: A patient engagement agent facilitated the creation and activities of the Committee. Ten HIV-infected individuals, recruited in 3 community organizations and 1 clinic, formed the Committee in November 2015 for two years, including 5 men and 5 women representing the main groups affected by HIV in Quebec (MSM, women, IDUs, immigrants from endemic countries). Main activities include monthly meetings and participants are treated as partners in decision-making and knowledge-production. Members regularly complete a short survey on their experience of meetings. The ethnography will draw on focus group transcripts, meeting notes, and survey data to produce a realist evaluation of the intervention.

Discussion: Regular Committee meetings allow patients to validate all steps of the I-Score Study. These should improve the I-Score measure's quality, make it more patient-centred, and increase its benefits for HIV patients. Importantly, the intervention evaluation will provide a 'thick description' of a patient engagement project, the circumstances of its successes and pitfalls, and of how HIV patient expertise can be integrated into research.

SSP5.09

Engaging heterosexual men with HIV in prioritizing key messages about their community for exchange with policy makers and knowledge users

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Background: Heterosexual men living with HIV have been historically not been engaged by HIV researchers. At a 2012 peer-led summit, heterosexual men with HIV identified research and advocacy priorities for their community. As a follow-up, we held the 'Knowledge Dissemination and Key Issues Workshop', where participants distilled the priorities into key messages for future engagement with policy makers and knowledge users.

Methods: A knowledge dissemination event was planned by a collaboration of community members and academic researchers. With the assistance of AIDS Service Organizations, twenty-five heterosexual men with HIV from across Ontario participated in the event. Activities included a review of findings from the 2012 summit, presentations regarding the health of heterosexual men with HIV, and small and large group discussions. Notes taken during the discussions and the large group debriefings underwent content analysis.

Results: Findings from the presentations were distilled into 4 key themes: 1) Heterosexual men with HIV are not the negative stereotypes often portrayed by media; 2) Heterosexual men should be added to the list of priority populations when funding HIV research and services; 3) Heterosexual men are a heterogeneous group with intersecting vulnerabilities to health disparities; and 4) Heterosexual men with HIV want to work collaboratively with other communities and policy makers to inform HIV-related programming and policy. For each theme, actions required and key knowledge users to be engaged were identified.

Conclusions: The Knowledge Dissemination and Key Issues workshop provided heterosexual men with HIV a forum for identifying the most salient messages about their community and the steps required for future engagement with policy makers and knowledge users. These findings will be shared with these stakeholders at a future knowledge translation and exchange forum.

SSP5.10

Documenting best practices for scaling-up community based research

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Background: The Dr. Peter Centre (DPC) is a community-based health care organization that provides care and support to people living with HIV, who have complex social and health needs. A community-based research (CBR) partnership was established between the DPC, the BC Centre for Excellence in HIV/AIDS, as well as researchers and policymakers from across Canada to investigate the impact of the DPC on health care access and outcomes. While CBR has recently become more common, a model for best practices has yet to be established. This critical review of the CBR process addresses the gap within implementation science literature by documenting the successes and lessons learned to inform broader CBR scale-up, specifically when working with structurally vulnerable populations.

Description: With 2 years of informed research design led by the DPC, the CBR team received funding from CIHR and MSFHR in 2012 to initiate a mixed-methods evaluation of the DPC model. Community Advisory and Knowledge Translation and Exchange Committees were established to be involved throughout the process.

Progress: Data were collected over 3 years from a virtual cohort, a longitudinal prospective cohort, and qualitative interviews. Five Peer Research Associates (PRAs), three of whom were DPC clients, were hired to administer surveys. This critical review of the CBR process augments the findings from the DPC evaluation to improve opportunities for CBR scale-up.

Lessons Learned: The research team's experiences suggest that CBR, including PRA involvement, is an effective model for fostering trust among structurally vulnerable participants, and has the potential to translate their lived experiences into policy-relevant evidence. Suggestions

to streamline the partnership development between community members and researchers include adjusting timelines to merge approaches and priorities, and identifying common objectives and contributing strengths. The documentation of the successes and challenges overcome is essential for moving this research model forward.

SSP5.11

Anti-inflammatory Drugs to Prevent HIV-1 Infection: Role of Community Engagement

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Health intervention methods are most effective when there has been significant community engagement. Basic/clinical science studies can potentially have an important impact on target populations, therefore, discussing with community and have their input prior to designing the study can increase adherence to the study. Such strategies are particularly pertinent for health interventions surrounding stigmatized illnesses such as HIV infection. Community engagement is shown to stimulate dialogue, activate interest and participation, and help introduce evidence-based knowledge to potential participants and community members.

Our study aimed to develop a new avenue to prevent HIV by inducing an immune quiescence phenotype by using daily uptake of anti-inflammatory. In the early stages of the planning, a community meeting was organized between potential participants from a community in Nairobi, Kenya and the study team. Issues regarding the study design, drugs used, potential side effects, study duration, samples to be collected and sampling methods were addressed. Following this, a randomized double arm study was designed. The anti-inflammatory drugs selected were hydroxychloroquine (200mg/day) and acetylsalicylic acid (81mg/day).

The consultative meeting addressed queries among the community before study began and helped to strengthen the study design and methodology. Participants and their partners strongly supported the drugs chosen. Drugs were viewed as 'common' with no associated stigma unlike other HIV prevention efforts. Therefore, no issues about participating in this study were raised and recruitment for the study exceeded expectations. Participants felt comfortable taking the drugs to their home and take them on a daily basis. At the end of the study, we measured drug level, at two time points, for each participant. Adherence to study treatment was around 96% (5 undetectable /142 samples analysed).

Our study underlines the importance of community engagement and that designing basic/clinical study with the community is feasible and increases the strength of the study.

SSP5.12

Taking Culture Seriously in Biomedical HIV Prevention Trials: Promoting Meaningful Community Engagement in HIV Research

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Background: A substantial gap exists between widespread acknowledgement of the importance of incorporating cultural sensitivity as an integral component of community engagement in biomedical HIV prevention trials, and empirical evidence to guide the operationalization of cultural sensitivity in these trials. We explored how the mandate of cultural sensitivity is conceptualized and operationalized in biomedical HIV prevention trials.

Methods: We used qualitative meta-synthesis to: 1) form a research question, 2) systematically search the literature, 3) select articles for inclusion, 4) critically appraise the quality of included studies, 5) abstract data from the studies, and 6) synthesize the findings. We selected qualitative studies that used interview, focus group, or case study methods if they incorporated discussion of social, contextual, or cultural considerations in HIV prevention technology research from the perspective of trial volunteers, key community stakeholders and/or trial staff in locations of planned or completed trials, and were published in peer-reviewed journals. Two reviewers independently abstracted descriptive and substantive data from included articles and analyzed substantive data using thematic synthesis techniques.

Results: Across 29 studies, the majority (n=17) were conducted in resource-limited settings. Four overarching themes emerged: (1) semantic cultural sensitivity—challenges in communicating scientific terminology in local vernaculars; (2) instrumental cultural sensitivity—understanding historical experiences to guide tailoring of trial activities; (3) budgetary, logistical, and personnel implications of operationalizing cultural sensitivity; and, (4) culture as an asset. A few studies demonstrated sophisticated operationalization and analysis of cultural sensitivity, with many conceptualizing culture primarily as a barrier to be navigated.

Conclusion: Future investigations should address how sociocultural considerations are operationalized in HIV prevention trials in particular sociocultural contexts, and evaluate the effectiveness of the methods employed. Approaching culture as an asset in addition to a challenge, and allocating resources to effectively operationalize cultural sensitivity will support meaningful community engagement in HIV prevention research.

SSP5.13

Planning and Community Engagement for HIV Cure Research in Canada: A Collaborative Program Between National Research Teams and Key Populations

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Background: Two Canadian team grants aim to find a cure for HIV and contribute to global efforts to put an end to AIDS. Lifelong adherence to antiretroviral therapy (ART) can reduce morbidity and increase lifespan significantly. Toxicity, consequences of aging, and failure to extend benefits to the 37 million people living with HIV globally push the effort to find curative treatments and eliminate dependence on ART. There is consensus that cures for HIV are possible if collaborative research takes place. Although an international working group has called for collaborations between researchers, institutions and affected communities, much work remains to initiate these linkages in Canada.

Methods: We conducted the first organized effort to engage affected populations (including adults and perinatally infected adolescents and their parents) across Canada in research on HIV cure/remission. Our goals were to:

- Raise awareness about HIV cure/remission studies
- Inform populations about global and Canadian research
- Solicit feedback on how to conduct the research
- Plan for sustainable community engagement

We conducted privacy protected in-person meetings in Montreal (11/2014), Toronto (01/2015), and Vancouver (04/2015) using community facilitators and electronic surveys subsequently distributed among participants.

Results: Stakeholders expressed enthusiasm for a sustained interactive program but with a need to manage expectations regarding the difficulties of cure research. Participants encouraged study of population differences, e.g., based on sex and gender, genetics, and ethnicity. Participants recognized the importance of biological sampling for research but urged close relationships with communities to promote acceptability. All participants expressed an interest for capacity building to enhance engagement. Youth sought dedicated opportunities to engage and take on public education roles; youth also encouraged engaging them using social media.

Discussion: Wider public discourse regarding HIV cure research is necessary, including with transgender, rural, Aboriginal, and other Canadians. Future plans for community engagement are underway.

SSP5.14

Engagement and endorsement by a leading community organization facilitates research participation among people living with HIV and those at-risk in Ontario

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Background: Increasingly, community-based organizations are engaged in research studies that aim to improve the lives of people with HIV and those at-risk, but these contributions are not well understood. We explored how engagement and endorsement by community organizations may facilitate participation in health research studies for people with HIV and those at-risk.

Methods: Participants recruited through Ontario community-based agencies completed peer research associate-administered questionnaires collecting information on sociodemographics, social determinants of health, importance of engagement and endorsement by a leading community organization, prior health research participation, and peer involvement. Univariate and multivariate logistic regression analyses were conducted to identify factors associated with willingness to participate.

Results: Of 1,011 participants, 539 (53%) were HIV-positive. Mean age was 44 years. 64% were men; 50% identified as LGBTQ; 62% were Caucasian, 19% Indigenous, 16% African, Caribbean, or Black. 621 participants (61%) expressed willingness to participate in health research in the future. Engagement and endorsement by a leading community organization (OR: 3.59, 95%CI: 2.42-5.34) and presence of a community advisory committee (OR: 3.49, 95%CI: 2.39-5.09) were both associated with increased willingness to participate in future research. Other significant factors included older age, LGBTQ identity, lower income, being retired or on disability, living in Northern Ontario, HIV-positive status, and having previous research experience. Engagement and endorsement by a leading community organization remained significant (AOR: 2.21, 95%CI: 1.19 – 4.10) in adjusted models as did: older age (AOR: 1.56, 95%CI: 1.14-2.13), annual income less than $20k (AOR: 1.37, 95%CI: 1.01-1.86), living in Northern Ontario (AOR: 1.78, 95%CI: 1.13 – 2.80), being HIV-positive (AOR: 1.74, 95%CI: 1.20 – 2.51), and having previous research experience (AOR: 2.68; 95%CI: 1.62 – 4.46).

Conclusion: Our study demonstrates that engagement and endorsement by a leading community organization can play a key role in increasing one's willingness to participate in health research.

SSP5.15

More than one model?: Lessons learned from an evaluation comparing traditional and activity-based advisory board models for CBR

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HIV community-based research (CBR) in Canada involves directly engaging people living with HIV (PLHIV) and affected communities. CBR funding requires formal engagement of affected communities; teams use approaches ranging from community advisory committees (CAC) to "peer research assistants." However, not all CAC models may be suitable or desirable for all PLHIV, particularly those individuals who experience complex health issues, and other systemic and institutional barriers, such as accessibility concerns, ongoing drug-use, cognitive challenges, or stigma.

Our study uses mixed methods to compare and evaluate two CAC models for engaging PLHIV who use substances and have ongoing health problems – a traditional CAC and an activity-based CAC called "Research Rec(reation)" (Research Rec). Research Rec, housed at Casey House – a sub-acute HIV hospital - is a flexible drop-in approach that uses creative and participatory methods (Lego, murals, tea tasting/making, etc.) to promote and structure discussion. Intake interviews (n= 21) and participant evaluation surveys were administered at five sessions with participants who were recruited and self-selected into Research Rec or the traditional CAC. We assessed motives for joining, perceived level of participation and enjoyment of each session. The majority of participants were male (72.2%), White (77.8%) and rated their health as 'fair' or 'poor' (61.1%). Follow-up interviews were conducted with 11 participants from both models. Our analyses found that less than half of the Research Rec participants had advised on research previously, compared to 80% of the CAC participants. Drawing on both participants' perspectives and team discussion, we share our research rec model and present findings from our study. We consider: participants' reflections on motives and barriers for participation; meeting structure; and issues of accessibility for PLHIV in hospital who use substances. Our results support the development and implementation of flexible activity-based methods to engage a wider group of PLHIV in CBR.

SSP5.16

Developing a psychoeducational support group for serodiscordant couples: A collaborative, participatory approach

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Project History: As providers of mental health and social support services for people living with and affected by HIV in Toronto, we are attuned to the number of service users in mixed-status (serodiscordant) relationships. Given the gap in group-based support services geared towards serodiscordant partnerships, we conducted an online survey to assess their needs for support. We heard from sixty-seven respondents about their mixed-status experience, including length of time living with HIV, length of relationship, strengths and challenges, and access to support. In summer 2014, six serodiscordant gay male couples engaged in an evaluation project to develop, implement and evaluate an eight-week psychoeducational support group using a collaborative, participatory approach.

Intervention: The participating couples were instrumental to the development of the program. In planning sessions, they identified topics they wanted to discuss and how they wanted to evaluate the modules. The module topics selected by the group members included HIV 101, Sex and Intimacy (two parts), HIV Treatment, and Emerging Research, Social Effects of Being in a Serodiscordant Relationship, Exploring Roles in Your Relationship and Communication Stratetgies, HIV and Mental Health, and Aging with HIV. Group facilitators were selected from the research team.

Findings: Group members identified key elemets of a participatory project as Ownership, Flexibility, Active Engagement, Trust, Structure, and Accessibility/Equity. All stakeholders reported that the project was highly participatory in unique ways that pertained to the group process and research process.

Recommendations: Group members recommended that AIDS Support Organization (ASO) programming needs to be more inclusive of serodiscordant couples, particularly the negative partner. Specifically, they suggested offering emotional support (groups and counselling) as well as informational support (workshops). Feedback for adapting the psychoeducational intervention included providing a menu of topics and presentation styles for selectiong, holding a follow-up maintenance group, and engaging group participants in project dissemination.

SSP5.17

"What's Hot with Peer Researchers?" Results of the evaluation of an online talk show about HIV peer researchers as non-formal education

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Background: CIHR is promoting patient-oriented research (SPOR) which fits well the GIPA principles of meaningful participation of people living with HIV (PHAs) in HIV/health research. To this purpose, since 2011, Universities Without Walls (www.universitieswithoutwalls.ca) at the Ontario HIV Treatment Network (OHTN) has been gathering a training curriculum for HIV+ peer researchers (PRAs) using blended online (a/synchronous) and in-person modules and activities. We report here on one specific online intervention using a talk show format called "What's Hot with PRAs?" (WHPRAs).

Intervention: WHPRAs is *informal and distance learning,* a form of *knowledge into action* (Straus & Holroyd-Leduc 2008) that promotes *reflective practice* (Schön 1983). WHPRAs runs for one hour every month for a widely diverse audience. The topics addressed are suggested by the audience and include key HIV research issues such as payment equity, workforce security and advancement, and the flexible boundaries of peer researchers.

Evaluation: using an online evaluation tool, we assessed the online intervention in the following dimensions: accessibility, usability of topics, and appeal. We aggregated results by region and type of audience member.

Results: 298 people have attended the nine editions of WHPRA since July 2014. 146 people completed the evaluation; 43% researchers, 29% peer research associates and 28% included service providers, community members and community organizations. 61% respondents reside in Ontario, 27% in British Columbia and 9% in Eastern and Atlantic provinces. 96% respondents reported satisfaction with WHPRA and 94% find that WHPRA provides a flexible forum to discuss key issues affecting peer research associates. It is estimated that it takes 15 staff and guest hours to prepare one show. The gains include a) enhanced connection between peers, researchers and students across Canada, b) supporting existing community based research projects and c) a more reflective practice of the complexity of the work of, and with, peer researchers.

SSP5.18

Community-based research strategies for recruiting a diverse cohort of women living with HIV in Canada

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Background: Women are under-represented in HIV research, in part due to structural challenges to study recruitment. We describe strategies for recruiting women with HIV in the Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS).

Methods: CHIWOS is a community-based research study conducted *by, with* and *for* women with HIV, in collaboration with researchers, providers, policy-makers and communities. 1,425 women with HIV were enrolled from BC, ON and QC to complete questionnaires administered by Peer Research Associates (PRAs). Recruitment strategies included PRA-driven efforts, outreach to clinics and AIDS Service Organizations (ASOs), and online methods. Women were asked: *How did you hear about the study*? Analyses describe recruitment methods overall and by province and population.

Results: Of 1131 participants with valid data, 38% were recruited in ON, 31% BC and 31% in QC. 40% identified as Caucasian, 33% as African, Caribbean or Black (ACB) and 19% as Indigenous. Median age was 45 years (IQR: 37-51); 96% identified as cis-women. PRAs and other peers recruited 35% of participants, clinics 34%, and ASOs 19%. PRAs/peers were the predominant recruitment method in ON (49%), compared with clinics in BC (40%) and QC (43%). Nationally, PRAs/peers were more successful in recruiting women who were transgender (47%), LGBTQ (41%), current injection drug users (37%), *not* currently on ART (39%) and *not* receiving HIV care (54%). Clinics were more effective in recruiting younger women aged 16-29 (49%) and women who did not use HIV support services in the last year (50%). Recruitment methods were less effective in engaging women who were ACB, transgender, rural and/or not accessing HIV services.

Conclusions: Peer-driven methods and clinics are key to recruiting diverse women in community-based HIV research, along with ASO supports that create opportunities for peers to connect. Additional targeted strategies are required to better engage hard-to-reach women.

SSP5.19

The Meaning of "Community" and "Peers" from the Perspective of Those Affected by HIV

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Background: Community-based researchers typically define "community" and "peer" pragmatically as those affected by an issue. In this analysis, we focus on perceptions of "community" and "peer" by those defined by HIV community-based research as community members.

Methods: Focus group participants were selected from willing participants to a survey on factors influencing HIV research participation. They represent populations most affected by the HIV epidemic in Ontario, using gender, sexual orientation, HIV exposure, and ethnocultural origin as selection criteria. Separate focus groups were held for HIV+ and HIV- participants, and for different ethnocultural groups (White, Racialized, ACB, and Aboriginal). The focus groups were conducted at local sites (e.g., ASOs, libraries) in 3 Ontario cities. Participants discussed the meaning of "community" and "peer" and community and peer involvement in research. With permission, focus groups were audiotaped and transcribed. Transcripts were coded by pairs of peer research assistants and investigators, thematically summarized, and cross-population themes were discussed by the team.

Results: 60 participants participated in 10 focus groups, ranging from 3-10 in size. "Community" was perceived differently by groups – some had difficulty expressing any sense of what a "community" was, others described it as geographic entity (town), place of origin (e.g., reserve), neighbourhood or place where they socialized; while others had a sense of (dis)connection to a multi-layered identity group (e.g., "gay world," "LGBT Black community"), sometimes experienced online. "Peer" was understood as someone with similar life experiences or attributes (including age, gender, sexual orientation, experience of HIV), as well as a shared understanding of the world, and acceptance.

Discussion: Not surprisingly, community perspectives on the meaning of "community" and "peer" in research were complex: "communities" were viewed as emanating from intersecting networks, but those included/excluded depended on context, and could impose an essentialized identity. "Peer" was a fluid concept, but less problematic.

Everyday Actualities of Living with HIV
Vivre avec le VIH au quotidien

SSP6.01

Supporting PHA Employment Preparedness- Lessons learnt from Legacy Pilot Program

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Background: The Committee for Accessible AIDS Treatment (CAAT) Research: "When PHA becomes service providers" (2013) engaged 27 PHAs working in AIDS Service Organizations to identify challenges and corresponding strategies when PHAs take up service provider roles. A key gap identified was the lack of a resource that support PHAs to effectively explore their life goals and develop career plans. In response,CAAT engaged concerned stakeholders and agency partners to develop a new training program to supportEmployment Preparedness (EP) for PHAs.

Methodology: EP was a four-day program that used a holistic approach to address the cognitive, emotional and social needs of PHAs related to employment engagement and career planning. Day 1 engaged participants to examine their life journeys and life goals to make decisions about returning to work. Day 2 provided in-depth knowledge on income supports along the employment continuum. Day 3 and 4 focused on skill building on job search, resume development and job interviewing. 12 PHAs who were considering returning to work participated in the training. Post training evaluation survey and1-year follow up were conducted with participantsto assess their experience as well as change in employment status.

Results: 100% of participants found the training content useful and relevant.80%of participants reported increased knowledge and sense of efficacy in dealing with emotions related to returning to work, planning their finances andengaging in self care. 83% of participants reported increased knowledge of the Canadian employment culture and how to create or update their resume. 100% of participants found the training helpful in building their job-search skills.

Conclusion: A holistic approach that integrates life goal exploration, emotional decisional balance, financial planning and job search skills is helpful in supporting PHAs to evaluate and enhance their own readiness to transition to employment.

SSP6.02

Evaluation of Web-based tailored interventions to support PLHIV in the adoption of health promoting behaviours: an online randomized controlled trial (CTN 288)

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Background: Long-term antiretroviral therapy use, normal aging, and certain risk factors are associated with metabolic disorders that predispose persons living with HIV (PLHIV) to diabetes and cardiovascular diseases. The emergence and progression of these disorders can be prevented by adopting healthy behaviours. Based on the theory of planned behaviour, *TAVIE en santé,* a Web-based tailored intervention, was developed.

Objective: To evaluate the effectiveness of *TAVIE en santé* in order to support PLHIV in the adoption of healthy behaviors such as being physically active, following a healthy diet and quitting smoking.

Methods: An online randomized controlled trial is currently ongoing across Canada. To participate in this study, PLHIV must be: ≥ 18 years, able read/understand French or English, have access to the Internet. A convenience sample of 750 participants will be randomly assigned either to an experimental group (*TAVIE en santé*, n = 375) or to a control group (predetermined conventional health-related websites, n = 375) The adoption of health behaviour (smoking cessation or physical activity or healthy eating) is the principal outcome. Cognitions (intention, attitude, perceived behavioral control) are the secondary outcomes. All outcomes will be measured with a self-administered online questionnaire and collected three times: at baseline, three and six months post-baseline. Principal analyses will test differences between the two trial groups using Intention-to-Treat analysis.

Results: Recruitment began in November 2015. The study is currently promoted through health professional and community networks. Interested participants are invited to visit the study's website at www.lhivehealthy.ca.

Conclusion: This study will yield new results about the efficacy of Web-based tailored health behaviours change interventions in the context of chronic disease. *TAVIE en santé* could constitute an accessible complementary service in support of existing specialized services to support people living with HIV adopt health behaviors.

SSP6.03

Improving health and reducing comorbidity associated with HIV: a Web-based tailored intervention to help people living with HIV make healthy choices

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Background: In the domain of health behaviour change, the deployment and utilisation of information and communications technologies as a way to deliver interventions appear to be promising and has the potential to promote healthy behaviours. A Web-based tailored intervention, *TAVIE en santé*, was developed to support persons living with HIV (PLHIV) be more physically active, follow a healthier diet and quit smoking.

Objective: This presentation aims to demonstrate *TAVIE en santé*.

Methods: This intervention was developed through an Intervention Mapping framework and is based on the theory of planned behavior (TPB).

Results: *TAVIE en santé* is a Web-based tailored tri-component intervention addressing smoking cessation (SC), physical activity (PA) and healthy eating (HE). Each component (SC, PA, HE) is composed of seven interactive computer sessions lasting 5-10 minutes (total duration ≈50 min./component). The sessions, hosted by a virtual nurse, aims to develop and strengthen skills required for behaviour change. During a pre-intervention assessment, PLHIV will have to: 1) choose one behaviour they wish to modify (SC or PA or HE) and; 2) answer questions related to their attitude, level of perceived behavioral control and intention regarding the chosen behavior (TPB items). Based on the TPB items scores, three profiles (P) are generated by a computer algorithm for each component (SC, PA, HE). The number of sessions, theory-based intervention methods and tailored messages contents will vary according to the profile (P1 = low attitude/7 sessions; P2 = low perceived control/5 sessions; P3 = high intention/3 sessions). Access to *TAVIE en santé* is unlimited in terms of intensity and frequency of use; it is available in French and English.

Conclusion: The effectiveness of *TAVIE en santé* is currently evaluated in an online randomized control trial across Canada (CTN288). This intervention could constitute an accessible complementary service in support of existing specialized services.

SSP6.04

HIV Stigma and Suicide among Canadian Gay and Bisexual men living with HIV

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Objectives: HIV stigma is pervasive in Canada but little is known about its health effects, particularly among gay and bisexual men. In a national Canadian survey we measured experiences of suicide ideation and attempts among gay and bisexual men living with HIV, and the extent to which these experiences were associated with HIV stigma.

Methods: We used data from the Sex Now survey 2014/2015 – an online national survey of Canadian gay and bisexual men with 8037 respondents. The survey questionnaire was developed through community consultation. We restricted this study to participants that self-reported being HIV positive. We measured the association between suicidal ideation and attempts with four measures of HIV stigma: social exclusion, sexual rejection, verbal abuse and physical abuse.

Results: A total of 678 HIV positive men completed the survey (8% of total sample). Among this group, 22% (n=152) had serious thoughts about suicide and 5% (n=34) had attempted suicide in the last 12 months. Men were more likely to report suicide ideation and/or attempts if they had been diagnosed with HIV within the past 2 years (OR 2.2 95%CI 1.5 – 3.3). After adjustment for sociodemographic factors, suicidal ideation and attempts were associated with each of the four measures of HIV stigma: being excluded socially for being HIV positive (AOR 1.9 95% CI 1.3 – 2.9), rejected as a sexual partner (AOR 1.6 95%CI 1.1-2.3), verbally abused (AOR 2.9 – 1.9 – 4.5), and physically abused (AOR 4.1 95% 1.6 – 10.0).

Conclusion: Gay and bisexual men living with HIV experience significant levels of HIV stigma that heighten their risk for suicide. The findings affirm the need for targeted interventions to prevent suicide, particularly post HIV diagnosis, amid public health efforts to de-stigmatize HIV and mental illness.

SSP6.05

Life after HIV disclosure: Analyzing barriers to gender-based violence service provision for women who experience post-disclosure violence in South Africa

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Gender-based violence (GBV) service organizations play an integral role in providing treatment for female survivors of post-HIV disclosure violence in South Africa. The objective of this research is to increase knowledge about the barriers facing GBV organizations in providing adequate services for women who experience violence following disclosure.

While negotiating HIV disclosure, women often weigh the benefits of improved mental and physical health, as well as familial and community psychosocial support, against experiencing stigma, social exclusion and interpersonal violence (Norman et al., 2007:1777). In South Africa, young women are particularly vulnerable to HIV infection and GBV, as they are often predisposed to poverty, economic insecurity, and have limited sexual agency (Higgins et al., 2011).

Using qualitative data from semi-structured interviews with GBV service providers and policy advocates, this master's research project examined barriers to GBV services and vulnerabilities to violence for women who experience post-disclosure violence in South Africa. Although HIV infection as a consequence of violence against women is sufficiently covered by current research, gaps exist with respect to women's disclosure of HIV as a risk factor for experiencing violence, and the capacity of South African GBV organizations to support survivors of violence.

Preliminary findings indicate that the lack of integrated GBV and HIV treatment services, as well as poor referral pathways for reporting services (i.e. police or legal action), increases the risk of re-victimization for survivors of violence. Furthermore, stigmatizing behaviours from service providers along the referral pathway prevent many women from seeking additional care. This has shown to negatively affect HIV treatment adherence and compromises women's health.

This research would contribute to our understanding of the determinants of women's disclosure of their HIV-positive status, and the relationship between violence and HIV management in South Africa, of which disclosure is a fundamental component.

SSP6.06

Rethinking the experience of side effects in the context of HIV treatment: A qualitative study

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Background: Despite the availability of new ARVs and the simplification of treatment options, side effects continue to affect people living with HIV. Side effects negatively impact health, well-being, and quality of life. They also contribute to poor treatment adherence and treatment discontinuation. Qualitative studies published to date are almost exclusively focused on adherence. As such, they fail to capture the experience of side effects as a whole.

Methods: This two-year qualitative study was designed to gain a critical understanding of the experience of side effects. Semi-structured interviews were conducted with 50 participants. Each interview was audio-recorded, transcribed, and analyzed. Data analysis was conducted in accordance with the principles of grounded theory.

Results: Three main categories emerged from the data: 1) the side effects, 2) the experience, and 3) the connections. The first category highlights the importance of taking into account the context in which they side effects are experienced as well as the types and nature of side effects. The second category puts forward the idea that the experience of side effects is composed of three interrelated processes: becoming with, living with, and dealing with. Finally, the third category points to new connections that are formed with people, things and systems in the presence of side effects.

Conclusions: Our findings suggest that three levels of actions are needed: 1) broadening our understanding of side effects, 2) improving the response to side effects, and 3) demanding change – a change in discourse and culture.

SSP6.08

Ethical Challenges in Healthcare for People Living with HIV: Notes from Qualitative Field Research of HIV Healthcare in Manitoba and Newfoundland

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For many, HIV has become a chronic condition. As people living with HIV live longer lives, the healthcare they require is changing. Shifts in the provision of healthcare can have profound and unforeseen consequences on the experience of illness for people living with HIV. We will describe how broader social issues contribute to the ethical challenges of care in context specific ways in our multi-site study.

As part of a five-year, multi-provincial program of linked research projects, we are conducting a qualitative study of challenges in healthcare for people living with HIV at clinics in Newfoundland and Labrador, Manitoba and Ontario. Our institutional ethnographic approach involves interviews with people living with HIV and healthcare providers, observation of clinical encounters and analysis of medical records. We will present preliminary findings from Winnipeg, Manitoba (our second site) and discuss contrasts with our findings from Newfoundland and Labrador (our first site).

In Manitoba there are multiple complex social challenges experienced by the groups most affected by HIV, including Aboriginal communities, gay men, and immigrants. These challenges include addictions as a cross-cutting theme among various groups affected by HIV. In addition, unstable housing, poverty, intimate partner violence, colonization and sexism are salient issues related to the experiences of living with HIV and the health and access to care for Aboriginal people. There has been some success with using trauma-informed approaches and multidisciplinary teams to provide care to people living with HIV who are impacted by structural factors in Manitoba. Ethical issues that arise in this province will be explored, and contrasted with our findings from Newfoundland and Labrador where interdisciplinary teams work to address different challenges. Findings will provide insights into the ethical concerns raised in the domain of HIV healthcare from the perspectives of providers and people living with HIV.

SSP6.09

Characterizing the Disability Experience among Adults Living with HIV: A Structural Equation Model Using the HIV Disability Questionnaire

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Purpose: To describe relationships between dimensions of disability experienced among adults living with HIV.

Methods: We conducted a structural equation modeling analysis using data from

the HIV, Health and Rehabilitation Survey Study to determine relationships between dimensions of disability as measured in the HIV Disability Questionnaire(HDQ): i) physical symptoms/impairments, ii) cognitive symptoms/impairments, iii) mental-emotional health symptoms/impairments, iv) difficulties with day-to-day activities, v) uncertainty, and vi) challenges to social inclusion. First, we established a measurement model, mapping HDQ domain scores to represent disability dimensions, using confirmatory factor analysis. We considered a Root Mean Square Error of Approximation (RMSEA) of <0.05 as an overall indication of model fit. Next, we established a structural model, which assessed the relationships between the dimensions of disability, using path analysis. We classified standardized path coefficients of >0.2-0.5 as a medium and >0.5 a large effect. All models were built with Mplus software.

Results: Of the 931 adults with HIV in Canada who completed the HDQ, the majority were men (79%), taking antiretrovirals (90%) and living with >2 concurrent health conditions (72%). The measurement model had good overall fit (RMSEA=0.04). The structural model indicated that physical symptoms/impairments was a strong predictor of difficulties with day-to-day activities (standardized path coefficient: 0.537) and medium predictor of mental-emotional health symptoms/impairments (0.240) and uncertainty (0.361). Uncertainty was a strong predictor of mental-emotional health symptoms/impairments (0.529) and medium predictor of challenges to social inclusion

(0.378). The relationship from physical and cognitive symptoms/impairments to challenges to social inclusion was mediated via uncertainty, mental health symptoms/impairments, and difficulties with day-to-day activities (total indirect effect from physical:0.217; cognitive:0.175).

Conclusions: Uncertainty appears to be a key direct and indirect predictor of mental-emotional symptoms/impairments and challenges to social inclusion. These findings provide a basis for conceptualizing disability for adults with HIV and may highlight roles for rehabilitation.

SSP6.10

Room for improvement: Knowledge exchange needs of people living with HIV

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Background: Since 1990, CATIE has provided health information to people with HIV. Over that time, CATIE's programs have evolved to meet the changing information needs of people with HIV.

Purpose: In 2015 CATIE undertook a national needs assessment of people living with HIV in Canada. It was designed to describe the current knowledge needs of people with HIV and how these needs can be met.

Method: An online survey, promoted through multiple channels, assessed the information needs of people with HIV.

Results: In total, 438 people with HIV completed the survey. Participant demographics included:

- 6% men
- 3% age 46 and older
- 5% diagnosed within the past 10 years; 27% diagnosed 10-19 years ago; and 28% diagnosed 20 or more years ago
- 5% were under the care of a doctor for their HIV and 92% were on treatment.
- Participants reported a large need for information, 94% needing at least 'a little' information on HIV and 92% needing at least 'a little' information on HIV treatment.
- Participants ranked the importance of different HIV topics. High priority topics included: How to stay healthy; HIV and aging; HIV's effect on the body; and preventing HIV transmission.
- For HIV treatment information, high priority topics included: what I need to know about HIV treatment; what I need to know about HIV treatment if I have other health conditions; and how to deal with side effects.
- Participants also ranked the importance of different formats for receiving information. Priority formats were: the Internet; fact sheets; and brochures and pamphlets.

Conclusions: A high level of need for information on HIV and HIV treatment exists among people with HIV. The survey identified clear priorities on topic areas and preferred formats. These can be used to develop resources and tools that support people with HIV.

SSP6.11

Perspectives of People Living with HIV: Activity and Participation Needs When Living at a Distance From Specialized Services

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Background: Activity and participation needs of people living with HIV in Manitoba, outside of Winnipeg, are unknown. HIV services are Winnipeg-based, requiring people elsewhere in the province travel for access. Rehabilitation professions help people live optimally, however HIV specialists are typically located in urban centres. Barriers to accessing HIV services, when living in non-metropolitan areas, result in health disparity.

Objectives: The proposed study will (1) explore, identify and prioritize the rehabilitation needs from the perspective of people living with HIV, at a distance from HIV services, in Manitoba; (2) describe perceived barriers, resources and solutions to meeting needs, including access and use of technology; (3) describe study participants' characteristics; (4) describe patterns of need associated with characteristics, in context of living in non-metropolitan areas of Manitoba.

Methods: Up to 24 participants in Manitoba will be purposively selected from adults living with HIV outside of Winnipeg. In-depth interviews using a semi-structured guide will provide qualitative data about activity and participation in home, work and leisure activities. Self-report surveys will provide quantitative data about demographics, health and risk factors. Verbatim transcripts of interviews will be analysed using qualitative description, content analysis and *in vivo* coding. Descriptive analysis will summarize survey data. Joint display will provide a matrix of qualitative themes plotted with associated survey characteristics, to better understand emerging patterns.

Results: The needs assessment will result in understanding the participant perspectives of unmet needs in context. Participant characteristics will be represented with descriptive statistics. Merging of qualitative themes with quantitative description will illustrate emerging patterns of needs identified by participants.

Practice Implications: Results will guide the development of interventions tailored to needs. Identifying resources and barriers, including access to, and use of, technology will guide efforts to improve access to rehabilitation services for adults living with HIV.

Gay, Bisexual and other Homosexually Active Men
Guais, bisexuels et autres hommes homosexuels actifs

SSP7.01

The Sex, Me & HCV Project: Four Videos for GBMSM at Risk of HCV and HIV/HCV Co-infection, and Service Providers

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Objectives: To raise awareness about increasing incidence of hepatitis C virus (HCV) among HIV-positive and HIV-negative gay/bisexual/men who have sex with men (GBMSM) in Canada associated with sex and sexualized drug use. To introduce community members and service providers to four videos and companion resources produced for GBMSM at risk of HCV acquisition, which they can use in community HIV and HCV prevention programs and interventions.

Content: Sexually active GBMSM living with HIV are at heightened risk of HCV acquisition, and HCV infection poses serious health risks for HIV-positive men from these groups. Despite evidence of increasing incidence of HCV among HIV-positive and HIV-negative urban GBMSM over the past decade in first world settings, no social-media-ready and culturally appropriate education/prevention resources have been produced in Canada. This PHAC-funded project produced four short videos (2 mins each) intended to raise awareness among GBMSM of HCV as a sexually transmitted infection (and the potential for HIV/HCV co-infection, and HCV re-infection), associated with specific sexual environments and practices, including sexualized drug use and sharing during sex and drug use. The videos affirm the continued negative health effects of stigma experienced by GBMSM, present accurate information in a sex-positive and non-judgmental manner, focus on the risks associated with "sharing", and suggest health promotion strategies to reduce personal and community transmission of HIV and HCV, and promote wellbeing (i.e., safer sex and drug use). To increase the capacity of service providers to meet the sexual health needs of GBMSM, and in-particualr those living with HIV, the videos have been "packaged" into a training module containing background information, existing prevention resources, and practice guidance.

SSP7.02

Supporting Family Physicians to Provide Safe and Appropriate Care for Men who have Sex with Men: A Structural HIV Intervention

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Background: Vancouver Coastal Health (VCH)/Providence Health Care (PHC) Regional HIV Services are committed to implementing structural HIV prevention interventions that address the contexts within which health is produced and reproduced.

Gay, Bisexual and Other Men Who Sex with Men (gbMSM) frequently experience poorer health outcomes because of the stigma and discrimination they are confronted within society. When gbMSM access Primary Care there is a greater likelihood that this care is not meeting all of their needs.

By enhancing family physician (FP) knowledge and comfort to provide appropriate care for gbMSM we can start altering the structures and context within which gbMSM access health care, helping to reduce some of the HIV vulnerability gbMSM experience and encouraging access to HIV testing and treatment. Currently there are no continuing professional development options on this topic available in BC.

VCH/PHC partnered with UBC Continuing Professional Development to develop an accredited webinar and workshop to offer FPs tools, strategies and practices to provide care for gbMSM.

Objectives:

1. Support physicians to improve their ability to provide safe, competent care for gbMSM
2. Reduce gbMSM HIV vulnerability by increasing access to safe, competent primary care

Methods: The project has 4 phases: (1) identifying the learning needs of FPs, (2) developing the webinar and workshop curriculum, (3) delivering the webinar and workshops, and (4) evaluating, improving and expanding the project. Learning needs were identified using key informant interviews and focus groups. Change in knowledge, comfort and skills was assessed through pre/post surveys and sustained changes in practice will be assessed at 6 weeks and three months post workshop.

Results: 109 FPs have attended the workshop and/or webinar. Data demonstrate that average FP confidence, knowledge and skill levels increased at least 1 point post workshop. Qualitative feedback reflects a commitment by FPs to improve their practice.

SSP7.03

Is the Number of Sexual Partners Still Important fo Gay and Bisexual Men's HIV Prevention Programs?

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Background: Sexual behavior among gay and bisexual men (GBM) is changing in response to: 1) Treatment as Prevention programs, 2) findings that many new HIV infections arise in regular, rather than casual sexual partnerships and, 3) research indicating that not all condomless anal intercourse (CAI) represents high risk behaviour. These recent developments question the relevancy of prevention programs emphasizing GBM partner number reduction.

Methods: To address this issue we analysed recent male sexual partner distributions reported by 719 Vancouver GBM enrolled in the Momentum Health Study. Participants were recruited from February 2012 – February 2014 using respondent-driven sampling; analyses used RDS weights. Univariable and multivariable negative binomial regression analyses modeled number of recent male sexual partners with respect to substance use patterns, psychosocial characteristics & sexual behavior, while controlling for socio-demographic variables. Variables with $p<.05$ were included in the multivariable model, with final variable selection determined by the AIC.

Results: The sample was predominantly White and well-educated. Median age was 33 years. RDS-adjusted HIV prevalence was 23.0%. Multivariable analysis showed partner number significantly associated with CAI with sero-discordant and/or unknown sero-status partners (ARR=1.25**,** 95%CI=1.04,1.52), sex toys (ARR=1.30,95%CI=1.04, 1.63), attending group sex events (ARR=2.44, 95%CI=2.04, 2.93), receiving money for sex (ARR=2.45**,** 95%CI=1.90,3.17), using crystal methamphetamine (ARR=1.69, 95%CI=1.31, 1.98), poppers (ARR= 1.20,95%CI=1.02,1.41), and Ecstasy (ARR= 1.20, 95%CI=1.00,1.44), Sexual Sensation Seeking (ARR=1.03, 95%CI=1.01,1.06) and preferring top (ARR=1.21,95%CI=1.00,1.47) or versatile (ARR=1.29, 95%CI=1.08,1.54) anal sex positioning. Self-identification as bisexual, relative to gay, was a significant negative variable (ARR=0.55, 95%CI=0.44-0.69).

Discussion: Results indicate that number of sexual partners remains an important proxy measure for GBM high risk sexual behaviour. However, more nuanced measures of sexual behaviour focusing upon HIV sero-status, viral load and HIV treatment status, plus research on the underlying causes of partner distributions are needed to understand GBM sexual health and decision-making.

Intervention Based Research in the Social Sciences: Theories, Methodologies, and Outcomes La recherche interventionniste Intervention en sciences sociales : Théories, méthodes et résultats

SSP8.01

Peer Consultation Debriefing schematic for Navigating Emotional Triggers (NET): model from the MSAFIRI Study and ABRPO's Turning to One Another project

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Background: The MSAFIRI Study is based at the University of Toronto, in partnership with the African and Caribbean Council on HIV/AIDS in Ontario and Women's Health in Women's Hands CHC. This study aims at understanding the factors associated with HIV acquisition in African and Caribbean immigrant communities after arrival to Canada. Three community members were hired as Peer Research Associates (PRAs) to recruit participants in community-based settings. As study activities could trigger emotional events for PRAs and interviewees, the team partnered with the AIDS Bereavement and Resiliency Program of Ontario (ABRPO) to develop a debriefing process.

Method: In January 2015, ABRPO was invited to provide training on debriefing for MSAFIRI PRAs using their resource kit for peer engagement called "Essential Tools for Support and Stability" (ETSS), developed in 2011. Feedback from the PRAs highlighted challenges in applying these tools in their interactions with peers during data collection; they requested a visual tool to help navigate the debriefing process. MSAFIRI and ABRPO then collaborated with study PRAs, investigators and advisory committee members to discuss drafts of the debriefing schematic.

Findings: The Navigating Emotional Triggers (NET), a visual tool that drew on ETSS concepts such as bracketing, debriefing and Emotional First Aid, was developed to help PRAs manage emotional triggers while conducting study activities. The NET guides PRAs in assessing and utilizing their personal capacity to respond to participants' and their own emotional distress while engaged in HIV research projects. It outlines a series of sequential practices to apply within triggering situations.

Conclusion/Next Steps: The NET is a schematic that has been touted as useful and relevant. Based on interest expressed in further training from other PRAs, AIDS service organization workers and researchers, we will develop a structured evaluation to assess the effectiveness and acceptability of this tool.

SSP8.02

Exploring the role of meal provision in promoting health and wellbeing among structurally vulnerable people living with HIV who use drugs

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Background: Food insecurity is a product of and contributor to the structural vulnerability of people living with HIV (PLHIV) who use drugs, and has been shown to compromise their HIV-related outcomes. Consequently, mitigating food insecurity is an important component of effective service delivery to PLHIV who use drugs with the potential to produce comprehensive improvements in HIV-related outcomes. Located in Vancouver, Canada, the Dr. Peter Centre (DPC) is a community-based integrative health care facility for PLHIV with complex care needs that include two nutrient-dense high caloric meals a day with oversight by a dietician. This study examines the role of the DPC's food services in contributing to improved HIV-related outcomes among PLHIV who use drugs.

Methods: This study draws on data from 30 semi-structured qualitative interviews conducted with DPC clients. Eligible participants were living with HIV, at least 19 years of age, reported a history of drug use, had enrolled in the DPC on or after February 27, 2011, and had completed a baseline quantitative interview.

Results: Study findings demonstrate that food insecurity is pervasive among study participants due to the social-structural barriers to accessing food. Participant accounts illustrate that DPC nutritional services were critical in mitigating participants' food insecurity. These services were said to create security and regularity in clients' lives with daily nutrient-dense meals and through connections with staff who are attentive to client needs. In turn, findings demonstrate that improved nutritional outcomes led to increased tolerance and adherence to HIV and opioid agonist treatment, as well as optimal weight management.

Conclusion: Food services offered at the DPC positively impact health outcomes and promote self-management among clients, mitigating structural vulnerability within this population. Results of this study highlight the importance of providing nutritious, sufficient, and consistent access to food within targeted, multi-faceted interventions for PLHIV who use drugs.

SSP8.03

The Adaptability of 'The HIV Positive Sero-Status Disclosure Intervention/Model for African Caribbean and Black (ACB) Women' among other populations

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Introduction: 'The HIV Positive Sero-Status Disclosure Intervention/Model for ACB Women' was developed and pilot tested in 2008-2010, which revealed positive testimonials from participants who had successfully gone through the process and service providers and peers who implemented it. The intervention helped reduce stigma of the diagnosis, anxiety, isolation, and facilitate the ability to disclose to significant others in order to prevent secondary HIV transmission. Our team worked together to explore the adaptability of this model in meeting the disclosure needs of other populations.

Three focus groups were held in Toronto with heterosexual black men (n=9), gay men/MSMs (n=13), and youth 18-30 (n=6), two focus groups were held in the Niagara region with heterosexual men (n= 2) and gay men (n= 4), and 8 in-depth interviews in the Waterloo region. The research participants (n=42) identified facilitators and barriers to disclosure, as well as recommendations for an HIV disclosure support model. Findings were cross-referenced with the existing model.

Findings: An effective HIV disclosure support model was identified as one that allows for: a tailored response, cultural support, education, peer support, and individual counselling that explores motivations for disclosure, assesses potential outcomes, and addresses the identified facilitators and barriers to disclosure.

The facilitators to disclosure were identified as: learning to accept an HIV-positive diagnosis, feeling empowered, increased knowledge and awareness of HIV/AIDS, support from organizations, peer support, and the opportunity to help others. The barriers to disclosure were identified as: ignorance and stigma, lack of support networks and or resources, fear of rejection, internal stigma, privacy concerns, the criminalization of HIV non-disclosure and culture.

Conclusion: 'The HIV-positive Sero-Status Disclosure Intervention/Model for ACB Women' encompasses the recommendations of an effective HIV disclosure model outlined by the research findings; indicating the utility of this model in addressing the HIV disclosure needs of other populations.

SSP8.04

The McLaren blueprint: Investigating the impact of supportive housing on the health and well being of people living with HIV in Vancouver, British Columbia

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Issues: McLaren Housing Society of British Columbia (BC) provides secure, affordable housing and support services for individuals and families affected by HIV throughout BC. In 2013 McLaren opened the Howe Street Residence, a 110-unit supportive housing complex. At its inception, there were no mechanisms for rigrous evaluation of this new residence, presenting a missed opportunity to demonstrate the impact of this intervention.

Description: The *At Home At Howe* study was designed by researchers at the BC Centre for Excellence in HIV/AIDS (BCCfE) in partnership with McLaren Housing Society to monitor the implementation of this housing complex on a prospective cohort of people living with HIV (PLHIV) at risk of homelessness. Two 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, participants are asked to complete a 1-hour peer-administered survey, which includes questions concerning the impact of the housing intervention on health and well-being. A linkage to the BCCfE will continue beyond the 24-month study period, providing a longer history of changes in adherence to treatment, regimen changes and clinical outcomes, as well as vital statistics and healthcare utilization. Survey data will be contextualized by semi-structured qualitative interviews.

Lessons Learned: Early PRA engagement with the residents encouraged rapid enrollment into the study. The peer-based model has helped garner trust amongst the participants, which may increase the disclosure and validity of self-reported information. The Howe street staff has been instrumental in engaging clients with multiple barriers to participate in the study.

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.

SSP8.05

Developing a Trauma Intervention for Women Living with HIV – Team Building and Pilot Development

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Literature has demonstrated that women living with HIV are much more likely to encounter traumatic stressors and have a diagnosis of posttraumatic stress disorder than women in the general population (Machtinger, Wilson, Haberer, & Weiss, 2012), and trauma and PTSD have negative impacts on health status and health care utilization for people living with HIV (Leserman et al., 2005). Additionally, women living with HIV report high levels of perceived stigma, potentially exacerbated by their experiences of trauma, which may impact their ability to seek appropriate health care services and receive social support (Wagner et al., 2010). Although trauma-focused treatments have been piloted with people living with HIV (Pacella et al., 2012), interventions to address traumatic stressors, and simultaneously increase resiliency, enhance social support, and reduce the impact of stigmatizing experiences have not yet been developed for women living with HIV. Clinical interventions for trauma often do not account for the needs of clients and front-line providers, creating a significant gap in translating research into practice. This presentation examines the development of a trauma intervention for women living with HIV in Toronto that is community-informed, evidence-based, and feasible within existing service structures. The presentation will discuss the formation of the team, the results of a community meeting, and the fusing of evidence-based traumatic stress interventions with the practical needs and the intersectional experiences of women living with HIV in Toronto.

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

An Evaluation of Peer Engagement within Fife House: Successes and Challenges of PHA Involvement as Volunteers

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Background: Greater and meaningful involvement of people living with HIV/AIDS (PHAs) can only be achieved through shifts in organizational cultures, by involvement

of PHAs in programs. Results of the needs assessment for the Peer Engagement Project (PEP) revealed that while volunteer engagement provides opportunities for personal growth, enhances self-esteem and reduces social isolation, volunteer work assigned often did not fit with levels of skills, experience and expectations. Effective engagement also requires developing consistent structures of support. The evaluation of this project aimed to assess the level of peer involvement as well as identify challenges and successes of the project and areas for growth.

Methods: Quantitative and qualitative methods were used to collect data for the evaluation. This presentation is based on the qualitative data collected from Peer Mentors, peer volunteers (active and inactive) and staff (with high and low levels of involvement with PEP), focusing on the successes and challenges in the implementation and execution of the project.

Findings: Challenges: Concerns of staff about conflicts, privacy and access to information restricted the opportunities for engagement of peers, creating barriers in providing meaningful engagement. Others challenges included: Recruitment and retention; Limited mentorship for peer volunteers; and Issues of boundaries within multiple roles (as client and as service provider).

Successes: Return to work was an empowering experience for many peers; Engagement as volunteers provided opportunities for developing connections and enhanced personal growth/skills; Comprehensive training program for PHA volunteers, staff support, supervision and accommodation contributed to their learning experience.

Recommendations: Develop more effective systems to match the interests, skills, and opportunities for peer volunteers; Include peer volunteers in developing future peer-based programs; Greater emphasis in trainings on conflict resolution, boundaries and management of multiple roles and; Debriefing should be included as an intrinsic part of peer engagement, distinct from ongoing job supervision.

SSP9.02

HIV and STBBI Testing: The Implications for Shifting and Socially Constructed Policy Environments

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Background: The Public Health Agency of Canada's shift to an integrated approach to STBBI prevention has the potential to profoundly impact the landscape of HIV and STBBI testing in Canada. In order to promote effective integrated prevention and testing responses, this study explored the potential consequences of integration from the perspective of stakeholders in the province of Nova Scotia. In addition, this study set out to stimulate and/or support potential responses to these consequences.

Methods: Guided by a social constructivist framework, this qualitative study drew on two forms of data collection and analysis. The first was a scoping policy analysis of documents related to the provision of HIV and STBBI testing in Nova Scotia. The second was two rounds of semi-structured interviews with eight participants, who included service providers, representatives of community-based organizations, and policy or government-level decision makers from Nova Scotia. Data were analyzed iteratively using a thematic analysis approach, with an emphasis on exploring how participants' disciplinary perspectives influenced their perception of integration and its consequences.

Findings: Through the analysis of first-round interviews, three key intersecting themes regarding integration and its consequences were identified. These themes included integration as promoting (or reducing) efficient responses, integration as an opportunity to reduce HIV stigma and normalize testing, and the need for high-level leadership to promote integration within a non-integrated system. During the second round of interviews, strategies for mobilizing action on the potential consequences of integration were further developed.

Conclusion: Successfully transitioning to an integrated approach to STBBI prevention requires increased collaboration between the sectors, organizations, and government departments that comprise the HIV and STBBI testing response in Nova Scotia. This presentation will conclude with a discussion of the strategies described by participants, and of the ongoing knowledge translation and mobilization activities associated with this study.

SSP9.03

Adapting to a Changing Landscape: Developing Living Positive Victoria's 2015-2017 Community Engagement Strategy

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Communities Deliver, a recent report by UNAIDS and Stop AIDS Alliance 2015, states that "while the core functions of the [community-based HIV] response remain essential, community systems are being challenged to adapt to changing service models and demands from funders." (2015, p. 4). Living Positive Victoria (LPV), a community-based HIV/AIDS organization (CBAO) echoes this sentiment and has developed a 2-year Community Engagement Strategy that reflects the diversity of people living with HIV (PLHIV) in the Australian state of Victoria; that details how LPV is currently succeeding at engaging Victorians living with HIV; and that provides recommendations to improve the organization's relationship with the communities it seeks to represent.

Utilizing a snowball sampling methodology, fifty participants (representing people living with HIV, members, volunteers, staff, and partner organizations) participated in individual and small group semi-structured interviews. The data was analyzed using NVivo software and a draft report was created. Member checking was then utilized to ensure

that participant responses were correctly summarized in the final report.

The report identifies seven themes, six areas of strength, five areas of improvement, and four recommendations for Living Positive Victoria to better engage diverse communities. Many of the themes emanating from the interviews point to the systemic challenges faced by PLHIV who are not considered part of the 'majority of PLHIV' and the imperative to invest in processes of critical self-reflection in order to ensure continuous quality improvement. The findings from this report and the process used to develop it are transferable to Canadian community-based HIV/AIDS organizations and have important implications for these organizations as they face the challenging reality of adapting to the changing landscape of HIV and other STIBBVs.

SSP9.04

Plugging into the Circuit Board: a collaborative role for research and communications in circulating HIV-related knowledge among community-based constituents

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To varying degrees, all AIDS service organizations (ASOs) interpret, assess and mobilize knowledge, which they share among their communities of knowledge users. However, most ASOs do not have the formal resources to systematically execute this task. Consequently, many ASOs and their staff may not benefit optimally from new information that may improve their ability to meet the changing needs of their service users and other stakeholders. We will explore a basic needs approach to addressing this challenge.

The basic needs approach comprises efforts to keep people abreast of developments within their field, rather than fulfilling higher-level information needs. Stakeholders may then selectively track the information through other channels that facilitate or support higher-order needs such as program and policy development. Within this approach, we will assess the role and function of community-based research and communications, and propose a joint role for research and communications in community-based knowledge mobilization and dissemination.

ASO stakeholders – mainly community-based practitioners, program planners, service users, and priority populations affected by HIV – enhance their grasp of HIV-related issues through reliable access to knowledge that has been assessed and communicated by a credible source within their community of practice. Decision-makers will further assess knowledge or evidence to determine whether or how it may support program or policy development.

Within this basic needs framework, a collaborative process for mobilizing and sharing knowledge includes integrating the following functions: locating and assessing research; identifying and prioritising issues that are relevant to different ASO stakeholders; prioritising which information needs may be fulfilled during specific time periods; determining what to communicate and in what form for various stakeholders; developing the content of the relevant stories; and pushing stories/issues, pulling audiences to a curated portal, and exchanging knowledge via channels best suited to the issue, form of output, and intended audience.

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

SSP10.01

Latino Trans Women Support/Psychoeducational Group

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Summary: HIV/STI's are common among Trans individuals (who do not conform the gender social norms). In Canada there is a gap in understanding the sexual health issues of Latino Trans Women. Therefore, there is a gap of services tailored for this particular group.

Theoretical Issues: Due to the impact of the Social Determinants of Health (Education, Race, Gender, Migration, Social Exclusion), those particular individuals do not have access to the same (sexual and mental) health services when compare to their gender-conforming pairs.

Stigma, discrimination, Transphobia and ignorance are prevalent among larger Spanish-speaking communities, affecting Trans Women's wellbeing.

There is a lack of role models about how to be a Latino Trans Women; therefore, there is a constant conflict of identity, high-risk sexual health practices and access to specialized health literacy.

Discussion: A support group with a number of 4-10 members has been celebrated weekly, for 8 sessions. Participants, have recruited hard-to-reach other members. Creating a first opportunity for Latino Trans Women sexual-mental health services. They are traditionally excluded from the community at large and practically invisible within the LGBTQ communities, due to their non-conforming gender characteristics, and due to their racial-ethnic background.

Lessons Learned:

- There is a lack of information of the real population size of Latino Trans Women in Ontario.
- They have a lack of role models (family, culture and communities), this exposes them to a higher risk of lower sexual health literacy, and higher risk to HIV/STI's.

- In addition, it has been found that higher levels of social isolation and mental health issues affect Latino Trans Women.

Recommendation: There is an urgent need for developing services for Latino Trans Women, particularly, developing and creating safe spaces for sexual and mental health discussion programs. More research needs to be taken place in order to better understand their specific needs.

Social, Structural and Systemic Drivers of HIV
Moteurs sociaux, structurels et systémiques du VIH

SSP11.01

PrEP Promise and Peril: The Regulatory Pathways to Equitable, Affordable and Timely Access in Canada

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Objectives: To increase knowledge of regulatory processes Truvada as HIV PrEP must go through in order to get to those who need it most in Canada. To increase awareness of opportunities to address structural and institutional barriers to PrEP access in Canada.

Content: PrEP (pre-exposure prophylaxis) has great potential to reduce HIV acquisition by people at heightened HIV risk. In August 2015, Gilead Sciences applied to have Truvada approved for HIV PrEP in Canada. People at risk and people working in HIV prevention (e.g., testing, PEP, risk reduction counselling) are likely asking or being asked: *How can I get PrEP? How much will it cost?* The answers are not simple or clear. Complex structural and institutional factors that trace the fault-line of health inequity in Canada may keep PrEP out of reach of marginalized people who could benefit most—including low income people, Aboriginal people, GBMSM, and sex working people. Based on published info sheets that policy-makers and service-providers can use in their work, this session will build knowledge, awareness and capacity. It will explain the current state of PrEP access in Canada; the regulatory pathways to expand access to PrEP; drug approval and public formulary listing; provide a "best estimate" timeline for public formulary listing of Truvada for PrEP; and identify Canadian practice guidance. The session will highlight policy considerations and outstanding questions that can pave the path to equitable, affordable and timely access to PrEP in Canada.

SSP11.02

Strategies Addressing Intimate Partners Violence (IPV) Among Women in sex work - Incremental Reporting of Intimate Partner Violence Interfaced with HIV Risk

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Background: Women in sex work (WSW) are subject to varied forms of violence, especially from intimate partners. WSW's vulnerability to violence and its interface to HIV/AIDS highlight the mechanisms by which the two interact. Lack of perspective among WSW on IPV and poor reporting poses significant challenges to HIV prevention & care programs. Hence community driven strategies were implemented to reach out 38000 WSWs aimed at improving their perspectives on IPV in Karnataka, India.

Methods: With support from University of Manitoba and UN Women, Project Samvedana was conceived to address elimination of violence against women in sex work in the state of Karnataka, India. The intervention was designed in consultation and active participation of women in sex work. Key focus of the intervention was to improve perspectives about IPV and rights of WSW.

Results: Looking at program monitoring data across three years of implementation indicated incremental reporting of IPV.

- September 2012 to August 2013 shows 27% WSW reported IPV,
- September 2013 to August 2014 shows 44% WSW reported IPV and
- Sept 2014 to July 2015 (till the end of the program) showed 48% WSW reporting IPV.
- The data prior to August 2013 showed WSW reported only violence perpetuated by external structures like police, goons, etc.
- Significant improvement were reported in access to HIV care and support services.

Conclusions: Improving perceptions about IPV leads to decreased vulnerability to HIV. Community led interventions have better impact in reducing violence and thus reducing HIV transmission.

SSP11.03

Addressing HIV/STI vulnerability: Applying the minority stress model to understand safer sex practices among lesbian, bisexual, and queer women

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Background: Approximately one-fifth of lesbian, bisexual, and queer (LBQ) women have a lifetime history of sexually transmitted infections (STIs), similar to heterosexual women. However, perceptions of low risk have limited our understanding of safer sex practices among LBQ women. The minority stress model has been used to explain that sexual stigma contributes to sexual risk practices among men who have sex with men. Scant research, however, has examined the relationship between sexual stigma and safer sex practices among LBQ women. Thus, we applied

the minority stress model to explore associations between sexual stigma and safer sex practices among LBQ women.

Methods: We explored associations between sexual stigma and safer sex practices among LBQ women. We also tested the interaction between sexual stigma, social support and resilient coping in this relationship. A cross-sectional internet-based survey was administered to 466 LBQ women in Toronto, Canada.

Results: Among 388 participants with complete measurement data, simple linear regression indicated both perceived and enacted sexual stigma were positively associated with uptake of safer sex practices. In multivariable analyses, significant interactions were found between perceived sexual stigma and resilient coping, and between enacted sexual stigma and social support. At low levels of social support, higher levels of enacted sexual stigma correlated with fewer safer sex practices, while at high levels of social support the relationship was reversed. At low levels of resilient coping, higher levels of perceived sexual stigma correlated with fewer safer sex practices, while at high levels of resilient coping the relationship was reversed.

Implications: Our findings document complex relationships between sexual stigma dimensions, coping, social support and safer sex practices. Understanding the role these variables play in uptake of safer sex practices can inform sexual health interventions tailored for LBQ women that aim to reduce the rates of HIV/STIs among this underserved population.

SSP11.04

Social Determinants of Health as drivers of the HIV epidemic: An ethnographic analysis of the HIV-related needs of African refugee women in Toronto

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There is sufficient evidence that shows that the social determinants of health (SDOH) are key drivers of the HIV/AIDS epidemic. But can the SDOH help us to better understand the HIV-related needs and priorities of African refugee women in Canada? How are the social conditions of African refugee women affecting the way they think about their sexual health, personal relationships, and intimacy, and how can HIV prevention in general be more attentive to refugee health and its determinants?

This presentation draws on multi-sited ethnographic observations and autobiographical narrative to explore the HIV-related attitudes and health practices of African refugee women living in Toronto.

The presentation will critically appraise (a) the links between pre-migration health experiences and the HIV-related health practices of refugee women living in refugee shelters in Toronto, Ontario, (b) the role of gender-based violence in refugee women health-seeking behaviors, and (c) refugee attitudes and responses towards HIV prevention in Toronto.

The presentation uses a rich auto-ethnographic approach to critically examine the social conditions that shape how African refugee women experience their health, and their HIV-related attitudes and practices. It will draw on personal life stories to unpack African refugee experiences and the role of HIV prevention within African refugee communities in Toronto.

SSP11.05

Hammer and Baton in synergy: Forging Strategic Partnerships to reduce violence and stigma against Female Sex workers

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Background: Women Sex Workers in India are victims of Poverty, exploitation, and trafficking. Gender Based Violence by family, society and state actors enhances vulnerability to HIV and critical infections and deprived human rights and dignity. Sensitizing law enforcing agencies to safeguard health, dignity and rights of female sex workers was essential.

Methods: Project Samvedana implemented by Karnataka Health Promotion Trust, funded by UNWomen aimed at reducing violence against sex workers in Karnataka state, India. Advocating with the State's Judicial Academy and the High Court, 400 judges across the state were sensitized on violence against Sex Workers. These judges headed District and Sub district Legal Services Authority. Advocacy with sensitized District Legal Services Authority led to partnerships in training police. 1567 policemen were trained in ten districts.

Results: Pre-Post evaluation indicates significant change in knowledge and attitude of Judges:

- "Can FSWs be punished for practicing Sex Work?" knowledge improved from 42% to 76%
- Acceptance of Sex Work as profession increased from 39% to 57%
- "Promoting condoms promotes promiscuity" belief changed from 36% to 21%
- Distinction between HIV/AIDS improved from 59% to 97%

Among Police

- Acceptance of violence on Sex Workers as "inevitable" decreased from 67% to 55%
- Belief "Sex Workers should be treated with dignity" improved from 66% to 83%
- Impact: Police violence decreased 17% to 7%

Conclusion:

- Forging strategic partnerships influences violence reduction, HIV and assertion of rights.
- Enhanced qualitative interface between Police, Judiciary and community creates enabling atmosphere.
- Sentized judiciary and police personnel treat sex workers with dignity.

The Medico-Legal Borderland: Criminalization, Law, Policy and Resistance
La frontière médico-légale : Criminalisation, droit, politique et résistance

SSP12.01

"Maybe if I stop the drugs, then maybe they'd care?" -- Hospital care experiences of people living with HIV who use substances

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Background: Hazardous drinking and illicit drug use (substance use) is associated with barriers to accessing and continuity of care, sub-optimal medication adherence, negative health outcomes and poorer quality of and satisfaction with care. Little is known about the experiences of people living with HIV (PHAs) who use substances during hospital stays. These data are required to inform interventions and quality improvement initiatives for these patients. We conducted a qualitative study characterizing the experience of accessing and receiving acute care in PHAs who use substances.

Methods: PHAs self-reporting an active substance use history at the time of an admission to an acute care hospital were recruited in Toronto and Ottawa. Data were collected through semi-structured interviews. Interviews were audio-recorded and transcribed. Data were analyzed inductively.

Results: 24 adults (19 men, 5 women) participated in the study. Participants recounted experiences of stigma and difficulty accessing desired care. Participants reported varying strategies to navigating the acute care system ranging from accessing care exclusively at hospitals where substance use was not believed to be recorded in medical charts to explicitly informing the clinical team of their substance use behaviours and needs (i.e., history of addiction, drug of choice, tolerance level). Inadequate pain management, withdrawal and boredom led to instances of leaving against medical advice, requesting drugs from visitors, and psycho-active drug use that was not prescribed during admission. Even when directly observed by staff, psycho-active drug use was rarely acknowledged by health care providers or discussed with patients.

Interpretation: PHAs perceived their historical and current substance use to be a barrier to seeking, accessing and continuing appropriate hospital-based care. Interventions to decrease stigma, improve pain management and drug substitution options, and increase the clinician-patient dialogue regarding substance use are necessary to improve the quality of care and care experiences of those who use substances.

Substance Use, Transmission Networks and Local Contexts of HIV Risk
Toxicomanies, réseaux de transmission et contextes locaux du risque concernant le VIH

SSP13.01

Exploring the influence of racial discrimination and HIV-related stigma on quality of life among African, Caribbean and Black women living with HIV in Ontario

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Background: African and Caribbean Black (ACB) women in Canada are disproportionately impacted by new HIV infections. ACB women's HIV vulnerabilty is shaped by contexts of stigma and discrimination. HIV-related stigma compromises quality of life (QOL) among women living with HIV (WLWH). Racism is associated with deleterious health impacts, yet scant research has explored racism and QOL among WLWH. We located no studies that examined concomitant effects of racial discrimination and HIV-related stigma on QOL. We explored the relationship between HIV-related stigma, racial discrimination and QOL among ACB WLWH.

Methods: We used data from a cross-sectional survey with ACB WLWH in Ontario (n=173) to test a conceptual model of pathways between HIV-related stigma, racial discrimination, depression, social support and QOL. We conducted structural equation modelling using maximum likelihood estimation to test the model.

Results: In independent models, HIV-related stigma and racial discrimination were associated with lower QOL, and depression partially mediated the associations between HIV-related stigma/racial discrimination and QOL. In the simultaneous model, HIV-related stigma had significant direct effects on depression, social support, and an indirect effect on QOL. Racial discrimination had significant direct effects on HIV-related stigma, depression, social support, and an indirect effect on QOL. When social support was added as a mediator, the direct effects between HIV-related stigma/racial discrimination and QOL were no longer

significant, suggesting full mediation. The model fit the data well (CFI: 0.929, TLI: 0.912, RMSEA: 0.071).

Conclusions: We found that racial discrimination was associated with higher HIV-related stigma, and HIV-related stigma and racial discrimination were directly associated with increased depression and reduced social support. The effects of HIV-related stigma and racial discrimination on QOL were mediated through social support and depression. Findings highlight the need for multi-level interventions to challenge intersectional stigma/discrimination, treat depression, and build social support, to improve QOL among ACB WLWH.

SSP13.02

Co-morbidity burden in persons with HIV originally from Africa and the Caribbean: a population-based study

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Background: In 2009, African, Caribbean and Black people represented approximately 19% of persons with HIV in Ontario and 23% of new diagnoses between 2001 and 2010. However, there are no studies quantifying comorbidity in this population. Accordingly, we compared rates of comorbidities between people with HIV originally from Africa and the Caribbean (AC) with HIV-negative individuals from these regions and people with HIV who were long-term residents of Ontario, between April 1, 2010 and March 31, 2013.

Methods: We used Ontario's health administrative databases and the Citizenship and Immigration Database. We used Poisson regression to compare rates of mental health illness, cardiovascular disease, chronic obstructive pulmonary disease (COPD) hypertension, diabetes and malignancy between our populations of interest.

Results: During the study period, we identified 1,525 AC persons with HIV. Compared with HIV-negative AC individuals (n = 228,925), AC persons with HIV had higher rates of COPD [adjusted rate ratio (aRR)1.78; 95% confidence interval (CI) 1.36 to 2.34), malignancy (aRR 1.20; 95% CI 1.19 to 1.43) and hospitalizations for mental health illness (aRR 3.33; 95% CI 2.44 to 4.56), diabetes (aRR 1.37; 95% CI 1.09 to 1.71) and hypertension (aRR 1.85; 95% CI 1.46 to 2.34). Compared with persons with HIV who were long-term residents of Ontario (n = 11,931), AC persons with HIV had higher rates of hypertension (aRR 1.91; 95% CI 1.78 to 2.05) and diabetes (aRR 1.62; 95% CI 1.51 to 1.74).

Conclusion: AC persons with HIV in Ontario are disproportionately hospitalized for conditions that could be managed in outpatient settings and have higher rates of COPD than HIV-negative AC individuals. These findings highlight where interventions are necessary to optimize the health of AC people with HIV.

SSP13.03

Health service use in persons with HIV originally from Africa and the Caribbean: a population-based study

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Background: In 2009, African, Caribbean and Black people represented approximately 19% of persons with HIV in Ontario and 23% of new diagnoses between 2001 and 2010. However, there are no studies examining health service use in this population. Accordingly, we compared health service use among people with HIV originally from Africa and the Caribbean (AC) with people with HIV who were long-term residents of Ontario, between April 1, 2010 and March 31, 2013.

Methods: We conducted a population-based study using Ontario's health administrative databases and the Citizenship and Immigration Database. We used Poisson regression to compare rates of emergency department use, ambulatory care visits and hospital admissions between our populations of interest. We conducted separate analyses for HIV-related and HIV-unrelated health service use. The research team included health care providers and frontline service workers.

Results: During the study period, we identified 1,525 AC persons with HIV. Compared with AC persons with HIV, people with HIV who were long-term residents of Ontario had higher rates of all-cause hospital admissions for any cause [adjusted rate ratio (aRR) 1.18; 95% confidence interval (CI) 1.07 to 1.31), emergency department visits (aRR 1.81; 95% CI 1.73 to 1.90) and ambulatory care visits (aRR 1.26; 95% CI 1.25 to 1.28). These results were similar when considering health service use related to HIV infection, with the exception of HIV-related outpatient use, which was lower among long-term residents of Ontario with HIV

relative to AC individuals with HIV (aRR 0.93; 95% CI 0.91 to 0.95).

Conclusion: With the exception of HIV-related ambulatory visits, AC persons with HIV use fewer health services overall than long-term residents of Ontario with HIV. The reasons for and implications of these differences require further study.

SSP13.04

En Avant: Implementing an Impact-Focused HIV/AIDS Research Strategy for African, Caribbean and Black Communities in Ontario

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Background: In 2013, African, Caribbean and Black (ACB) communities are disproportionately impacted by HIV in Ontario, representing about 15% of new infections. Yet, there is a dearth of research to understand the issues underlying this trend and inform responses. In 2012, the African and Caribbean Council on HIV/AIDS in Ontario (ACCHO) held the 3rd Ontario ACB Research Think Tank (RTT3) to identify research priorities. This led to the *En Avant* initiative to engage community, clinical and research leaders in the co-design of HIV research concepts and plans for how they will collaborate to develop them into full proposals for submission to grant competitions.

Methods: ACCHO and the Ontario HIV Treatment Network commissioned a planning committee to design a process for rapid generation of concepts for research proposals that align with priorities identified in the Ontario HIV/AIDS Strategy 2025 and the Ontario HIV/AIDS Strategy for ACB Communities 2013-2018, focusing on the three major themes from the RTT3: (1) evidence-based practices, (2) clinical and immunological issues and (3) methodological innovations.

Results: *En Avant* was initiated at a one-day convention of leaders from across Ontario, which yielded eight research concepts. A follow-up plan was created to support leaders to maintain momentum in developing their concepts into HIV research grant proposals. Potential support strategies include facilitating mentorship of new researchers and preparing a best practice resource on conducting research with ACB communities. Identified next steps include strategizing a plan for ensuring sustainable community-ownership of the initiative by transitioning leadership of *En Avant* to the ACCHO Research Committee.

Conclusions: *En Avant* is a long-term, strategic, and coordinated effort to bring together community and research leaders to champion the acceleration of ACB HIV/AIDS priorities' translation into research action. It enhances the ACB research agenda and strengthens evidence-based responses to HIV in ACB communities in Ontario.

SSP13.05

"I have no small vision for this group": (non)Disclosure and Stigma in Positive African Women's Mobilizing in a Prairie Urban Centre

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In this presentation we examine the ways in which African immigrant women living with HIV organize support and care in the form of a "support" group. In this space, they leverage resources, come to terms with seeking support and care, and establish family-like supports amidst ongoing trajectories of family disruption due to HIV and war-ridden displacement. Amidst sustained experiences of stigma the "women's group" provides social and symbolic resources to cope with living with HIV in a new socio-cultural context. This coming together has encouraged the women to take a step further to become critical catalysts against HIV stigma. A discourse of disclosure as liberation is commonly promoted among people living with HIV. However, the different positions the women find themselves in show the contradictions of this discourse when stigma is an inevitable experience as they have to draw support from small tightly knitted immigrant communities. When the women examine each other's social positions, the political mobilization they hope the group to achieve reaches an impasse. As a social response to HIV stigma this group of women embarked on a research project to mobilize their stories for change and to break that impasse. As much as dissemination in the "right" places may foster improved responses to human rights abuses they face; once again, the stigma associated with HIV continues to halt women from fully taking charge of the dissemination of the project, showing some of the limitations of community-based research as truly democratic process. Yet, a few women have creatively found ways for drawing attention to the research findings in public spaces where professionals and community members meet to discuss HIV. By going off the script of regular dissemination research processes, this unconventional approach remains grounded in the women's realities while opening up our understanding of CBR in HIV.

SSP13.06

Meaningfully Engaging Heterosexual Black Men in Responses to HIV in Ontario: Lessons from weSpeak a Critical Community-Based Research Program

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HIV/AIDS research and programs have been slow to meaningfully engage heterosexual Black men in responses to and prevention of HIV. Additionally, Black communities are often skeptical of participating in research which historically have been, and currently are, frequently exploitative and not beneficial to the wellbeing of Black communities. In particular, Black men experience stereotypes and prejudicial beliefs stemming from legacies of colonial research and the history of the enslavement of people of African descent. Therefore, developing trust and buy-in from Black men to participate in research can present significant challenges for researchers.

weSpeak: Straight Black Men Building Resilience to HIV in Ontario is a 5-year program of research and related activities with African, Caribbean and Black (ACB) heterosexual men in Ontario to: understand their vulnerability to HIV in relation to individual and structural factors; promote resilience and strengthen their commitment to HIV prevention; and strengthen community networks to end HIV and promote health among ACB communities. This presentation reports on innovative strategies used by weSpeak in four cities in Ontario - Windsor, London, Toronto, Ottawa – to meaningfully engage ACB men and communities in multiple stages: community outreach and promotion, establishment of local advisory committees, participant recruitment, data collection and ongoing structured communication. Our approach promotes: (1) meaningful engagement of heterosexual ACB men and communities underpinned by principles of social justice, equity and commitment towards collective self-determination; (2) capacity building in all engagement processes; (3) use of communication strategies that attract the attention of diverse ACB people; and (4) understanding and action on critical health literacy and the social determinants of health.

Preliminary findings suggest the importance of consistently ensuring greater and meaningful involvement of people living with and affected by HIV and supporting leadership roles for ACB stakeholders, designing research to address community priorities.

SSP13.07

Knowledge Translation of HIV Research with Policy-Makers, Health Workers, and the Media in Sub-Saharan Africa: Successes and Lessons Learned

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Background: From 2013-2015, Grand Challenges Canada funded the adaptation of the Canadian Evidence-Informed E-Module on HIV Rehabilitation into an open access teaching tool for rehabilitation providers in Sub-Saharan Africa (ssa.hivandrehab.ca). In December 2015, the product was launched in 6 countries targeting health workers, policy-makers and the media.

Objective: To reflect on the successes and lessons learned about the widespread knowledge translation efforts for the launch of a novel HIV teaching tool for rehabilitation providers in Sub-Saharan Africa.

Process: The E-Module was launched in Cameroon, Kenya, South Africa, Zambia and Canada on World AIDS Day 2015. The E-Module includes 5 sections addressing: (1) the role of rehabilitation in HIV in Sub-Saharan Africa; (2) what rehabilitation providers need to know about HIV in Sub-Saharan Africa; (3) rehab interventions to help adults living with HIV, (4) rehab interventions for children and youth living with HIV, and (5) tools for measuring rehab outcomes. The launch included multiple knowledge translation strategies. Press releases were developed and individualized for each of the 5 countries, including quotes from local team members. A formal press event was convened by the University of Zambia (UNZA) Public Relations Department, which included the study team as well as faculty from the UNZA Department of Physiotherapy. A community-based workshop was convened in Cameroon to promote anti-stigma efforts while launching the teaching tool. Two universities in South Africa collaborated on the release. Partners in Kenya convened a capacity-building workshop. A commentary was published in the Toronto Star.

Conclusion: Having trusted, long-term local partners greatly facilitated planning and extended the reach of the knowledge translation efforts to facilitate awareness of the HIV E-module teaching tool. Engaging formal communications expertise and support from University of Toronto, UNZA, and the Canadian Working Group on HIV and Rehabilitation (CWGHR) was instrumental in guiding the process.

The Health of African, Caribbean and Black Communities
La santé des collectivités africaines, antillaises et noires

SSP14.01

Awareness of the Supreme Court ruling on HIV non-disclosure among people living with HIV who use illicit drugs in a Canadian setting

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Background: In 2012, the Supreme Court of Canada (SCC) ruled that people living with HIV (PLWH) who did not disclose their serostatus before sex that posed a realistic possibility of HIV transmission could face criminal charges. Awareness of this ruling among marginalized PLWH remains undefined.

Methods: Participants of the AIDS Care Cohort to Evaluate Survival Services, a cohort of community-recruited PLWH who use illicit drugs in Vancouver, presenting for semi-annual follow-up between June-October 2015, completed a supplemental survey. The primary outcome was self-reported awareness of the SCC ruling on HIV non-disclosure. We determined sources of information and completeness of understanding of the legal obligation to disclose. Multivariable logistic regression identified factors independently associated with awareness.

Results: Among 249 participants (39% female), median age and years living with HIV were 50 (IQR: 44-55) and 15 (IQR: 10-20), respectively. Overall, 45% (n=112) reported awareness of the ruling, of whom 39% (n=44) reported a complete understanding of the legal obligation to disclose. Participants learned about the ruling from newspapers/media, healthcare providers, friends, and AIDS Service Organisations (reported by 46%, 27%, 21% and 20%, respectively). Among participants aware, 51% reported that no healthcare providers had talked to them about disclosure and the law. However, 56% of all 249 participants reported that they would feel comfortable talking to their regular HIV physician about this. Awareness was negatively associated with HIV viral load suppression (<50 copies/mL) (AOR: 0.51, 95% CI: 0.27-0.97) and positively associated with recent condomless sex vs. no sex (AOR: 2.00, 95% CI: 1.03-3.92).

Conclusion: Most participants were not aware of the 2012 SCC ruling. Discussions about HIV disclosure and the law were lacking in healthcare settings, despite most participants expressing a willingness to receive this information from HIV physicians. Clarifying providers' role in educating PLWH about HIV disclosure and the law is critical.

SSP14.02

Women and HIV: The realities of violence and criminalization

Melissa Medjuck, Donna Tennant, Sangam G, Erin Seatter

Positive Women's Network, Vancouver, BC

Issue: Disclosure continues to be a very difficult issue for women living with HIV (WLHIV). Stigma leads to fears about disclosure. After telling partners about their HIV+ status, WLHIV report facing rejection, shaming, blame, lack of confidentiality, and ostracism by community; losing financial support, shelter, and child custody; and experiencing abuse. WLHIV experience more frequent and severe abuse than HIV-negative women. Criminalization of non-disclosure adds another layer of complexity. WLHIV report being threatened and blackmailed with nondisclosure allegations by abusive partners, and service providers in the HIV and anti-violence sectors lack knowledge about nondisclosure legislation and the connections between HIV and gendered violence.

Description: Positive Women's Network (PWN) is the longest-running women-specific HIV organization in Canada. PWN and Battered Women's Support Services co-organized a forum in December 2015 in Vancouver. It included an interactive workshop on violence and HIV, a lecture on nondisclosure legislation, clips from the Legal Network's documentary films, and a panel of 5 WLHIV discussing real-life experiences. 80 participants attended.

Lessons Learned: Drawing on group discussion and evaluation forms, most participants were service providers in the anti-violence or healthcare sectors who were not aware of nondisclosure legislation or had little understanding of the legislation as well as the intersections between violence and HIV.

Challenges: Nondisclosure legislation is complex and ever-changing; a small number of women are able and willing to speak publicly about violence and the impacts of nondisclosure legislation; basic HIV education is needed before exploring nondisclosure legislation; limited time for discussion; education does not address systemic forces that perpetuate stigma and gendered violence.

Next steps: Results indicate a need for more education on HIV, gendered violence, and nondisclosure legislation. Advocacy efforts to promote justice, autonomy, and safety for WLHIV and amendments to nondisclosure legislation are proposed.

Social Sciences Other
Sciences sociales, Autre

SSP15.01

Towards Greater and More Meaningful Involvement of PHAs: An Evaluation of the Impact of Peer Engagement Project

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Background: The needs assessment for PHA engagement project recognized that meaningful engagement reduces isolation and positively impacts self-esteem. To enhance the greater and meaningful involvement of people living with HIV/AIDS (PHAs), the Peer Engagement Project aimed to increase the number of peers involved within Fife House; and reinforce and strengthen Fife House's commitment to GIPA/MIPA. Peer Engagement Project was a four year project aimed at developing training, structured mentorship support and experiential learning opportunities for PHAs. This evaluation aimed to assess peer involvement within Fife House Peer Engagement Project (PEP) and its impact.

Methods: Both quantitative and qualitative methods were used to collect data. Participants in the evaluation included Peer Mentors, peer volunteers (both active and inactive) and staff (both with high and low levels of involvement with the peer engagement project). This presentation specifically focuses on the impact of peer engagement on the peer volunteers and the organization.

Findings: Secondary data shows that the number of peer volunteers contributing to Fife House programs and services increased from 7 in 2010 to 65 in 2014, contributing approximately 2868 hours in 2014. Peer engagement positively impacted PHAs decisions to return to school, volunteer at other places, find employment and to seek further learning opportunities. Engagement of peers at Fife House also had a positive impact on their self-esteem, ability to relate to others, emotional health and increased their social connectivity. For Fife House, engagement of peers was instrumental in developing a comprehensive training program and new service initiatives, thus strengthening the agency resources.

SSP15.02

When Less is More: The Pruning of Social Networks by HIV-Positive Older Adults

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Background: The number of older people in Canada living with HIV has doubled in the past 20 years. Research shows that social support is an important part of aging well with HIV, contributing to quality of life and resilience, and serves as a protective factor against stigma and other stressors. Larger and more inclusive social networks are often seen as beneficial, however the quality of network relationships needs to be considered.

Methods: Using qualitative methods, in-depth interviews were conducted with 30 adults, age 50 and over, self-defined "aging well with HIV", living in Ontario, Canada. Interviews were conducted between February and May of 2013. Participants were recruited through ASOs, clinics, and HIV service providers. Participants discussed intrapersonal and interpersonal attributes contributing to successful aging. Open and thematic coding was undertaken by the researchers, and through consensus, four themes were identified and associated with successful aging.

Results: Respondents reported that the quality of social relationships was more important than the quantity in helping them age successfully with HIV. Pruning, or the cutting away of non-supportive network members through selection, was a central theme that emerged from the data. The phenomenon of pruning included: 1) appraisal of the relationship, 2) keeping out the negative, 3) letting in the positive and 4) fortifying the self. Participants actively removed relationships that detracted from their well-being. Pruning resulted in being able to focus more on the few close, enriching relationships, which led to "quality over quantity".

Implications: The quality of the relationships in the lives of older HIV-positive Canadians is an important element to consider. Older adults living with HIV may need support to eliminate non-healthy or non-supportive individuals from their networks in order to age successfully.

SSP15.03

The Benefits of Summer Camp in Building Self-esteem and Resilience with HIV-affected Children and Youth

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Background: Children living with and impacted by HIV exhibit increased symptoms of stress/anxiety, depression, and low self-esteem. Multiple strengths-based programs to support school-aged HIV-affected children have been initiated in Canada, including two residential summer camps – Camp Moomba (CM) in British Columbia (since 1998) and Teresa Group Summer Camp (TGSC) in Ontario (since 2013). We describe the outcomes of camp evaluations with respect to benefits of attending camp.

Methods: TGSC conducted Camper and Counselor evaluations as well as parent surveys post-camp at the end of 3 consecutive camps (2013-2015). Qualitative data regarding

camper experiences were collected by CM over 4 years for program assessment.

Results: Approximately 40 campers attended TGSC each year and 95-100% completed end-of-camp evaluations. Campers consistently reported improvements in developing interpersonal relationships, gaining skills and confidence through trying new activities and learning independence by being away from home. Many campers reported that they had learned respect, how to be a good listener, the importance of being kind and caring and the value of "talking things out". Counselors felt the top benefits to campers were in personal development, positive social interactions and new experiences. Parents were impressed with their children's personal advancements, including improvements in responsibility, independence, leadership and self-confidence and were pleased their children had opportunities to engage in new activities independently. CM, which hosts approximately 40 campers per year, identified similar themes in their evaluations, with campers particularly valuing increased peer support and opportunities for peer education.

Conclusions: Camp programs offered to youth in Ontario and British Columbia are shown to positively impact campers' lives by building supports, improving life skills, and allowing campers to have fun. Physical activities, interpersonal skills-building, leadership programs, and group activities in a camp setting serve to develop children's self esteem and resiliency in the face of HIV-related stigma.

SSP15.04

Supporting local community capacity building to serve newcomer PHAs across Ontario, lessons learnt from the provincial HIV and Immigration training program

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Background: Immigrants and refugees living with HIV/AIDS (IRPHAs) have accounted for 12-18% of new HIV cases annually in Canada since 2002. Ontario receives the largest proportion of newcomers in Canada (PHAC). The complexity and ever changing immigration systems in Canada have led to much confusion, fear and access barriers for newcomers and their service providers. In response, the Committee for Accessible AIDS Treatment (CAAT) work with various partners to organise HIV and Immigration training to promote service access competency amongst IRPHAs and service providers.

Methodology: A 12-member advisory committee with agency representatives from across Ontario was formed to guide the development, implementation and evaluation process of this program. A working group comprising of HIV and immigration legal experts and CAAT staff developed the core training curriculum, which is continually updated and adapted to reflect changing immigration legislations and based on specific needs and issues identified by service partners co-organizing the training in different regions. Evaluation data is collected from training participants to track outcomes and to inform continual improvement of the program.

Results: Since 2013, trainings have been conducted in 8 Ontario cities including both large urban centres and smaller cities. Over 100 participants attended the training with approximately 50% service providers and 50% PHAs, though proportion differs in each location.

Over 80% of participants found the training helpful and provided them with new and helpful information that would enable attitudinal and service delivery practice changes. The training also fostered partnership building and awareness of services provided by the HIV/AIDS Legal Clinic of Ontario with different regions.

Conclusion: This program has been effective in supporting local community capacity building to improve access through the complex immigration continuum. Continued partnership building amongst HIV, legal and settlement will further reduce access barriers and improve the health of newcomer PHAs across different regions.

SSP15.05

Evaluation of media coverage and publicity for "Je suis séropo," a Quebec anti-stigmatization communications campaign

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COCQ-SIDA, Montréal, QC

Background: Media campaigns play an important role in the fight against HIV stigmatization. Although confidentiality shapes the way HIV is spoken about in the media, some people living with HIV (PLWHIV) assert that this approach actually reinforces the stigma surrounding HIV. **In light of this, the "Je suis séropo" campaign gives a voice to the people most directly affected by stigmatization: PLWHIV.**

Description:

The campaign was launched across Quebec in 2012. The objectives of the campaign were

1) **to** demonstrate through testimonials that PLWHIV are people like anyone else.
2) to create a community of PLWHIV ready to speak publicly about their HIV status.
3 to launch the « je suis séropo » website.

Media coverage was measured through media monitoring, and an analysis of website traffic using Google Analytics.

Results: 5 PLWHIV agreed to be spokesperson for the campaign.

There were 47 traditional news stories published (newspapers, television, radio and online) in 6 regions of Quebec.

The www.jesuisseropo.org website received nearly 2,000 visitors between November 25 and December 2, 2012. By December 31, 2015, this number had reached 28,000.

Today, the community includes 11 PLWHIV.

Next steps: This initial evaluation demonstrates that the "Je suis séropo" campaign successfully engaged public interest, and gave PLWHIV a forum to speak. A next step might aim to evaluate how the spokespeople adopted the campaign and used the promotional materials.

SSP15.06

HIV Stigma and HIV Invisibility: Key barriers students' Readiness to Engage in HIV care and prevention education

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Background: Students at universities are seldom engaged in the HIV/AIDS response. HIV/AIDS services are not inclusive of their needs and priorities, which heighten the stigma, and undermine HIV testing, and other health promotion activities. To address this, National Youth Council (NYC) partnered with Makerere Institute of Social Development (MISD) to develop a study to address the gaps.

Methods: In 2014, NYC and MISD undertook a study to explore barriers and opportunities in addressing HIV and other health needs of MISD students in Kampala, Uganda. The project team consisted of student leaders from halls of residence, hostels, and faculty. 60 students from halls of residence, another 40 from hostels were recruited. Ethics approval was got from MISD research ethics council.

Results: Challenges identified were: (1) HIV invisibility among students (HIV is seen as a disease for the 'uneducated'); (2) fear to seek HIV testing due to perceived lack of confidentiality; (3) fear of rejection/shame and consequences of being associated with HIV/AIDS. The challenges and misconceptions of HIV affecting only specific groups reflect ideological barriers amongst students. It also reflects deep-rooted stereotypes and sense of 'othering' that impede HIV prevention and care initiatives. Potential strategies identified include: 1) HIV 101 packages for all returning students; 2); curriculum review/redevelopment to include HIV/AIDS in all courses; 3) periodic HIV and health forums on-and off-campus to address complacency related to HIV issues.

Conclusions: Ongoing engagement of students provides strategies to address gaps. Strategic opportunities on-and-off campus exists that can facilitate effective HIV prevention efforts. To address the barriers, the study recommends: a) expanding HIV testing/counselling facilities and HIV education during orientation week; b) university and student councils take up HIV/AIDS as an important community and health issue; c) multi-sectoral response to facilitate critical dialogue amongst students and faculty to address HIV knowledge gaps

SSP15.07

Case Study: CATIE's Hepatitis C Ethnocultural Education, Outreach, and Social Marketing Program

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Background: CATIE's Hepatitis C Ethnocultural Education, Outreach and Social Marketing Program is a hepatitis C awareness and educational outreach program for immigrants and newcomers in Ontario. The program works with four communities (Chinese, Pakistani, Punjabi and Filipino) and in four languages (Mandarin, Urdu, Punjabi and Tagalog).

The program addresses the hepatitis C health information needs of immigrants and newcomers. A case study has been developed to highlight the learnings of this project's first four years of work and frame the program models of community development and translation.

Purpose: In Canada, immigrants and newcomers are disproportionately affected by hepatitis C and hepatitis B. Immigrants and newcomers are estimated to represent 35 percent of all past or present hepatitis C infections in Canada. The primary mode of transmission for this group is unsafe medical practices outside of Canada, including transfusions of contaminated blood and reuse of unsterilized medical or dental equipment. Hepatitis C is not routinely screened for during the immigration process, so many immigrants may not know they have the virus.

Method: In the program's first four years, CATIE developed and implemented a multi-level strategy including three areas of work:

1. Education and outreach
2. Development and distribution of multilingual education resources
3. Media campaigns

The program takes a community development approach, which includes meaningful community involvement; engagement and partnerships with settlement, community and religious organizations; and a commitment to health equity.

Result(s): The program now has two effective models for **community development** and **translation** working with immigrant and newcomer communities. These models have produced ongoing partnerships, hepatitis C health information resources in 12 languages, an outreach and education program in four languages, and a social marketing campaign.

Evaluation and distribution metrics have also been collected for the last four years demonstrating effective engagement and reach in each of the communities.

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Consider a DOLUTEGRAVIR BASED REGIMEN for your HIV patients.

Triumeq®
dolutegravir/abacavir/lamivudine

The first and only single-pill regimen containing dolutegravir*†

Tivicay®
(dolutegravir tablets)

Offers a dolutegravir-only pill that can be used in combination with other antiretroviral agents

www.dolutegravir.ca

TRIUMEQ® is indicated for the treatment of human immunodeficiency virus (HIV-1) infection in adults. TIVICAY®, in combination with other antiretroviral agents, is indicated for the treatment of HIV-1 infection in adults and children 12 years of age and older and weighing at least 40 kg.

All patients should be screened for the HLA-B*5701 allele prior to initiating or re-initiating treatment with TRIUMEQ®. TRIUMEQ® is contraindicated in patients who are positive for the HLA-B*5701 allele and patients with a prior history of a hypersensitivity reaction to abacavir, or products containing abacavir, regardless of HLA-B*5701 status. Fatal hypersensitivity reactions have been associated with rechallenge of abacavir.[1]

* Comparative clinical significance is unknown.

† TRIUMEQ® is not recommended in patients requiring dose adjustments such as patients with renal (CrCl <50 mL/min) or hepatic impairment. The separate components should be used. TRIUMEQ® alone is insufficient for patients with integrase inhibitor resistance or when co-administered with efavirenz, etravirine fosamprenavir/ritonavir, tipranavir/ritonavir, oxcarbamazepine, carbamazepine, phenytoin, phenobarbital, St. John's wort or rifampin. Adjust dolutegravir dose to 50 mg twice daily (additional 50 mg dose of dolutegravir separated by 12 hours from TRIUMEQ®). TRIUMEQ® should only be used with etravirine when co-administered with atazanavir/ritonavir, darunavir/ritonavir or lopinavir/ritonavir in INI-resistant patients.

In studies supporting TRIUMEQ®, the individual products, TIVICAY® + KIVEXA®, were used.

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CA/DGR/0002/16–E Date: 03-2016

ViiV Healthcare
www.viivhealthcare.ca
ViiV Healthcare ULC

TRIUMEQ®

Indications and clinical use

TRIUMEQ® (dolutegravir/abacavir/lamivudine) is indicated for the treatment of human immunodeficiency virus (HIV-1) infection in adults.

Caution should be exercised in the administration and monitoring of TRIUMEQ® in elderly patients (≥65 years of age). The safety and effectiveness of TRIUMEQ® in pediatric patients (<18 years of age) has not been established.

Contraindications

In patients who are:

- hypersensitive to this drug or to any ingredient in the formulation or component of the container
- positive for the HLA-B*5701 allele and patients with a prior history of a hypersensitivity reaction to abacavir, or products containing abacavir, regardless of HLA-B*5701 status. Fatal hypersensitivity reactions have been associated with rechallenge of abacavir
- prescribed dofetilide

Most serious warnings and precautions

Fatal Hypersensitivity Reactions (HSRs): can occur at any time during therapy. Screening for the HLA-B*5701 allele prior to initiating or re-initiating treatment with TRIUMEQ® is required. Patients who carry the HLA-B*5701 allele are at high risk for experiencing a hypersensitivity reaction to abacavir, although, HSRs have occurred in patients who do not carry the HLA-B*5701 allele. Do not use TRIUMEQ® in HLA-B*5701-positive patients or in patients with a negative HLA-B*5701 status who had a suspected abacavir HSR on a previous abacavir-containing regimen. Regardless of HLA-B*5701 status, permanently discontinue TRIUMEQ® if hypersensitivity cannot be ruled out, even when other diagnoses are possible. NEVER restart TRIUMEQ® or any other abacavir- or dolutegravir-containing product in patients who have stopped therapy with TRIUMEQ® due to an HSR. Recognize that symptoms may lead to misdiagnosis of HSR as respiratory disease (pneumonia, bronchitis, pharyngitis), or gastroenteritis.

Lactic Acidosis and Severe Hepatomegaly with Steatosis: including fatal cases, have been reported with the use of nucleoside analogues. Discontinue TRIUMEQ® if clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity occur.

Severe Acute Post Treatment Exacerbations of Hepatitis B: have been reported in patients who are co-infected with hepatitis B virus (HBV) and human immunodeficiency virus (HIV-1) and have discontinued lamivudine. Hepatic function should be monitored closely with follow-up for at least several months in patients who discontinue TRIUMEQ®. Initiation of anti-hepatitis B therapy may be warranted.

Nursing Women: HIV-1-infected mothers should not breastfeed their infants to avoid risking postnatal transmission of HIV.

Other relevant warnings and precautions

- Potential for opportunistic infections and other complications of HIV infection
- Risk of transmission of HIV infection: appropriate precautions should continue to be taken
- Should not be administered concomitantly with other products containing abacavir or lamivudine (KIVEXA®, 3TC®, COMBIVIR®, HEPTOVIR®, TRIZIVIR® or ZIAGEN®) or emtricitabine-containing products (ATRIPLA®, COMPLERA®, EMTRIVA®, STRIBILD® or TRUVADA®)
- Risks of HSRs are associated with both abacavir and dolutegravir and share some common features such as fever and/or rash with other symptoms indicating multi-organ involvement
- Use of abacavir may be associated with a potential increased risk of myocardial infarction; underlying risk and modifiable risk factors for coronary heart disease should be considered when prescribing antiretroviral therapies, including abacavir
- Redistribution of body fat
- Pure red cell aplasia reported with lamivudine use
- Liver chemistry changes: increased risk for worsening or development of transaminase elevations in patients with hepatitis B or C co-infection receiving TRIUMEQ®; monitoring of liver chemistries is recommended
- Particular diligence should be applied in initiating or maintaining effective hepatitis B therapy in hepatitis B co-infected patients
- Close monitoring required with concomitant use of interferon alpha with or without ribavirin and TRIUMEQ®
- Risk of pancreatitis; discontinue use of TRIUMEQ® until diagnosis of pancreatitis is excluded
- Inflammatory response to indolent or residual opportunistic infection (IRIS); may include autoimmune disorders
- TRIUMEQ® should not be used in pregnant women unless the potential benefits outweigh the potential risk to the fetus
- If dose adjustments are required in patients with mild hepatic impairment (Child-Pugh grade A) then the individual components of TRIUMEQ® should be used; TRIUMEQ® is not recommended for use in patients with moderate to severe hepatic impairment (Child-Pugh grade B or C)
- TRIUMEQ® is not recommended for use in patients with a creatinine clearance < 50 mL/min. If dose adjustment is required in patients with renal impairment, the individual components of TRIUMEQ® should be used

Dosage and method of administration

Adults (≥18 years of age):

- The recommended dose of TRIUMEQ® is one tablet once daily.
- TRIUMEQ® can be taken with or without food.
- TRIUMEQ® is not recommended for patients requiring dosage adjustments, such as patients with renal impairment (creatinine clearance <50 mL/min) and patients with hepatic impairment.
- TRIUMEQ® alone is insufficient for patients with integrase inhibitor resistance requiring dolutegravir 50 mg twice daily.
- When TRIUMEQ® is co-administered with efavirenz, etravirine*, fosamprenavir/ritonavir, tipranavir/ritonavir, oxcarbamazepine, carbamazepine, phenytoin, phenobarbital, St. John's wort or rifampin, adjust the dolutegravir dose to 50 mg twice daily. The additional 50 mg dose of dolutegravir should be taken, separated by 12 hours from TRIUMEQ®.

*TRIUMEQ® should only be used with etravirine when co-administered with atazanavir/ritonavir, darunavir/ritonavir or lopinavir/ritonavir in INI-resistant patients

Adverse events:

Treatment-emergent clinical adverse reactions (rated by the investigator as moderate or severe) with a ≥2% frequency through 96 weeks of therapy in treatment-naive patients were: insomnia (3%), headache (2%) and fatigue (2%).

For more information:

Please consult the Product Monograph at triumeqpm.viivhealthcare.ca for additional important information relating to adverse reactions, drug interactions and dosing. The Product Monograph is also available by calling 1-877-393-8448. To report an adverse event, please call 1-877-393-8448.

TIVICAY®

Indications and clinical use

TIVICAY® (as dolutegravir sodium), in combination with other antiretroviral agents, is indicated for the treatment of human immunodeficiency virus (HIV-1) infection in adults and children 12 years of age and older and weighing at least 40 kg.

The following should be considered prior to initiating treatment with TIVICAY®: Poor virologic response was observed in subjects treated with TIVICAY® 50 mg twice daily with an integrase strand transfer inhibitor (INI)-resistance Q148 substitution plus 2 or more additional INI-resistance substitutions, including, but not limited to T66A, L74I/M, E138A/K/T, G140A/C/S, Y143R/C/H, E157Q, G163S/E/K/Q, or G193E/R.

Contraindications

- In combination with dofetilide.

Relevant warnings and precautions

- Potential for opportunistic infections and other complications of HIV infection
- Risk of transmission of HIV infection: appropriate precautions should continue to be taken
- Hypersensitivity reactions reported with integrase inhibitors. Discontinue use if signs and symptoms of hypersensitivity develop
- Liver chemistry changes: increased risk for worsening or development of transaminase elevations in patients with hepatitis B or C co-infection receiving TIVICAY®- monitoring of liver chemistries is recommended
- Particular diligence should be applied in initiating or maintaining effective hepatitis B therapy in hepatitis B co-infected patients
- Immune reconstitution inflammatory syndrome (IRIS): Patients responding to antiretroviral therapy may develop an inflammatory response to indolent or residual opportunistic infections, including autoimmune disorders
- Lipodystrophy/fat redistribution observed in patients receiving antiretroviral therapy
- Should not be used in pregnant women unless the potential benefits outweigh the potential risks to the fetus
- Not recommended in pediatric patients younger than 12 years or weighing less than 40 kg. Safety and efficacy of TIVICAY® have not been established in children less than 18 years of age who were infected with suspected or confirmed INI-resistant HIV-1 virus
- Nursing mothers should be instructed not to breastfeed if they are receiving TIVICAY®
- Insufficient study data to determine if patients >65 years of age may respond differently; caution should be exercised in dose selection for the elderly patients due to the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy

Dosage and method of administration

Recommended Dosing Regimen

Patient Population	Dose	Regimen
Adults and adolescents age 12 to 18 and weighing at least 40 kg		
Treatment-naïve*	50 mg	QD†
Treatment-experienced, INI-naïve*	50 mg	QD
Adults		
Treatment-experienced, INI-resistant‡	50 mg	BID§

* The dose of TIVICAY® is 50 mg twice daily when co-administered with potent UGT1A/CYP3A inducers, including efavirenz, tipranavir/ritonavir, fosamprenavir/ritonavir or rifampin.
† QD=once daily
‡ Alternative combinations that do not include metabolic inducers should be used where possible for INI-resistant patients. The safety and efficacy of doses above 50 mg twice daily have not been evaluated.
§ BID=twice daily

TIVICAY® can be taken with or without food.

Adverse events

The most common adverse reactions of moderate to severe intensity and incidence ≥2% (in those receiving TIVICAY® in any one study) are insomnia, headache, fatigue, nausea and diarrhea. The overall safety profile was similar across the treatment-naïve, treatment-experienced (and integrase-naïve) and integrase-resistant patient populations.

For more information

Please consult the Product Monograph at http://tivicaypm.viivhealthcare.ca for additional important information relating to adverse reactions, drug interactions, and dosing. The Product Monograph is also available by calling 1-877-393-8448. To report an adverse event, please call 1-877-393-8448.

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