## Advances in Technology and Virology

### 201

**HIV-1 AND HIV-1 TAT PROTEIN DOWNREGULATE IL-23 AND IL-27 EXPRESSION IN DCS**

Andréane Chénier [1,2]; Jonathan Angel [1,2,3]
1-Department of Biochemistry, Microbiology and Immunology, University of Ottawa; 2-Molecular Medicine, Ottawa Health Research Institute; -Department of Infectious Diseases, Ottawa Hospital

**Plain Language Summary:** Dendritic cells (DCs) are potent antigen presenting cells whose role in eliciting immune responses in the context of HIV-1 infection remains unclear.

**Objective:** To determine if HIV-1 modulates DC function by downregulating the production of IL-23 and IL-27, cytokines important in the generation of cellular immune responses.

**Methods:** To generate monocyte-derived DCs (MDDCs), freshly isolated monocytes were cultured for 6 days with IL-4 and GM-CSF. To determine the effects of an endogenous source of tat on cytokine expression, MDDCs were infected with a pLXIN (ptat) construct containing the HIV-1 tat wt gene or the empty vector for 24h, before a 4h LPS (1µg/mL) stimulation. To determine the effects of an exogenous source of tat, DCs were pre-treated with recombinant tat protein (rTat) for 1h before LPS stimulation. Alternatively, DCs were cultured in the presence of HIV-1 dual-tropic strain 92HT593 for 24h before LPS stimulation. IL-23p19 and IL-27EBI3 and p28 mRNA expression were evaluated by qRT-PCR and reported as relative expression levels.

**Results:** DCs are readily infected with the ptat, as shown by RT-PCR. The presence of endogenous tat resulted in a decrease in IL-23p19, IL-27 EBI3 and p28 mRNA expression. Incubation of DCs with rTat similarity decreases IL-23p19, IL-27 EBI3 and p28 mRNA expression. When cultured in the presence of HIV-192HT593, a similar downregulation in IL-23p19 and IL-27EBI3 was observed, with no significant effect on p28 expression.

**Conclusions:** HIV-1 tat protein, whether from an endogenous or exogenous source, significantly downregulates IL-23p19 and IL-27EBI3 and p28 mRNA expression. HIV-1 similarly downregulates IL-23p19 and IL-27EBI3, but seems to have no effect on IL-27p28. HIV-1 dysregulation of IL-27 subunits EBI3 and p28 and IL-23p19 may be a mechanism by which HIV-1 evades the infection-clearing immune response. Understanding the function of cytokines expressed and secreted by DCs to initiate T cell polarization may lead to better understanding of HIV-1 pathogenesis and the development of novel therapies for HIV infection.

**Contact Information:** Andréane Chénier, Tel: 613-737-8160, Email: achenier@ohri.ca

### 202

**ESTABLISHMENT OF A LEVEL 2 MOUSE MODEL FOR THE STUDY OF MICROBICIDE PREVENTION OF VAGINAL AND RECTAL HIV TRANSMISSION**

Amanda Harrison [1,2,3]; Clifford Lingwood [1,3]; Donald Branch [1,2]
1-Department of Laboratory Medicine and Pathobiology, University of Toronto; 2-Canadian Blood Services; 3-Hospital for Sick Children Research Institute

**Plain Language Summary:** Topical microbicides represent a simple way to prevent sexual transmission of HIV. The screening of potential compounds as microbicides is hindered by the lack of mouse model. We have therefore developed a mouse model of an HIV surrogate that can be used to screen potential microbicide compounds in a level 2 biosafety facility.

**Objective:** Sexual transmission of HIV continues exponentially and topical microbicides represent a simple way to prevent both vaginal and rectal mucosal infection. The lack of a mouse model for mucosal infection for use in facilities without biosafety level 3 represents a major obstacle in the screening of potential microbicide compounds. Therefore, we have developed a mouse model for the study of mucosal transmission of an HIV surrogate for use in a level 2 biosafety environment.

**Methods:** We use a pseudoenvelope-typed replication-deficient VSV-G/NL4-3luc HIV-1 virus that is approved for level 2 biocontainment. Both male and female CD1 mice were challenged rectally and vaginally with the pseudoenvelope-typed virus mixed into an FDA-approved cream for topical vaginal use. DNA from both vaginal and rectal challenged and unchallenged tissue was isolated after 2 hours. PCR and nested PCR was conducted to detect the reverse transcribed HIV-1 cDNA. Currently we are using this mouse model to test the efficacy of certain glycosphingolipid (GSLs) analogues, which we have shown previously to inhibit HIV-1 and pseudoenvelope-typed virus infection in vitro, to act as effective inhibitors of vaginal or rectal viral transmission.

**Results:** The pseudoenvelope-typed HIV-1 virus infects both rectal and vaginal mucosa in CD1 mice when challenged alone and when presented in cream format after 2 hour challenge. We have shown that the GSL, adamantylglobotriaosylceramide (ada-Gb3), a water soluble modification of kidney-derived Gb3, markedly reduced infection of Jurkat cells by the pseudoenvelope-typed HIV-1 virus. Ada-Gb3 is easily incorporated into a cream or gel and we have begun testing to determine if either can provide protection against mucosal infection.

**Conclusions:** This mouse model of HIV-1 mucosal infection using an HIV-VSV-G chimeric virus in topical format allows for the quick screening of potential microbicides in a Level 2 biosafety containment facility.

**Contact Information:** Amanda Harrison, Tel: 416-660-7999, Email: a.harrison@utoronto.ca

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### BIOMARKERS OF HIV DISCORDANT SHEDDING IN SEMINAL PLASMA USING A PROTEOMICS APPROACH

Shehzad Iqbal [1]; Prameet Sheth [1]; Desmond Persad [2]; Roberta Halpenny [2]; Colin Kovacs [2]; Rupert Kaul [1,3]
1-Clinical Sciences Division, University of Toronto; 2-Canadian Immunodeficiency Research Collaborative; 3-Department of Medicine, University Health Network

**Plain Language Summary:** Although most HIV transmission occurs through sexual intercourse, surprisingly little is known about what determines the levels of virus in the genital/rectal fluids. This is important to understand, as virus levels dictate how infectious an individual is to others. During ongoing studies of semen immunology in HIV infected and uninfected individuals, we identified a select group of individuals with no detectable virus in their seminal fluid, despite having high levels of virus in their blood (termed non-shedders). Conversely, we also studied individuals with abnormally high viral levels in their semen compared to blood (termed high-level shedders). We hypothesized that differential shedding of HIV in the semen of infected men might be related to levels of innate immune proteins in semen. Using a proteomics approach we have identified proteins which are associated with discordant shedding in the seminal plasma of these HIV infected individuals. Further characterization of these proteins may yield clues as to their potential role in viral shedding and importantly could aid in the development of novel inhibitors of HIV transmission.

**Objective:** In therapy naïve HIV infected individuals we analyzed the seminal plasma proteome of HIV non-shedders and high-level shedders, compared to normal shedding individuals, to find potential innate immune factors associated with HIV-discordant shedding.

**Methods:** We enrolled 28 participants and measured blood and seminal plasma viral load, identifying HIV non-shedders (n=6), high-level shedders (n=7) and normal shedders (n=15). Using surface enhanced laser desorption ionization-time of flight mass spectrometry (SELDI-TOF MS) we analyzed the proteome of the seminal plasma using a cationic exchange ProteinChip Arrays.

**Results:** Preliminary univariate analysis has revealed a 3.9 kDa protein that was under expressed in the high-level shedding individuals compared to normal shedders (p=0.01). In addition, a 28.2 kDa protein was under expressed in the high-level shedders compared to normal shedders (p=0.04) and non-shedders (p=0.02). No differences were seen between non-shedders and normal shedders.

**Conclusions:** Two biomarkers were under-expressed in participants with high-level HIV semen shedding. These may represent innate immune proteins important in the local control of HIV levels: the process of identifying these biomarkers is ongoing.

**Contact Information:** Shehzad Iqbal, Tel: 416-946-7054, Email: shehzad.iqbal@utoronto.ca

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### INCREASED FUNCTIONAL EXPRESSION OF MULTIDRUG RESISTANCE PROTEIN 1 (MRP1) IN CULTURED GLIAL CELLS TREATED WITH THE HIV-1 VIRAL ENVELOPE PROTEIN GP120 AND CYTOKINES

Patrick Ronaldson [1]; Christopher Tran [1]; Vijay Rasaiah [1]; Reina Bendayan [1]
1-Department of Pharmaceutical Sciences, Leslie Dan Faculty of Pharmacy, University of Toronto

**Plain Language Summary:** Mrp1 is an efflux pump that can export the antioxidant glutathione. Altered Mrp1 activity during disease may change glutathione levels in brain cells and contribute to brain damage by the process of oxidative stress. Our goal is to determine if toxic substances present in the brain during HIV-1 infection [i.e., HIV-1 viral envelope protein gp120, cytokines (i.e., TNF-α, IL-1β, IL-6)] can alter Mrp1 levels and activity. We observed that gp120 and TNF-α increased Mrp1 levels and activity in astrocytes, a type of brain cell that can be infected by HIV-1. We also showed increased glutathione export in gp120 exposed cells. These results imply that increased levels and activity of Mrp1 may contribute to the pathogenesis of brain HIV-1 infection.

**Objective:** Brain immunological responses are known to occur during HIV-1 encephalitis (HIVE). Using an in vitro model of HIVE-associated immune responses, we demonstrated that TNF-α, IL-1β, and IL-6 secretion is mediated by an interaction between gp120 and CCR5. However, it is unknown if the functional expression of Mrp1, an efflux transporter involved in the extrusion of physiologic substrates such as glutathione (GSH) and glutathione disulfide (GSSG), is altered in this model system. Altered GSH/GSSG export may disrupt cellular redox equilibrium and contribute to oxidative damage during HIVE. Our goal was to investigate Mrp1 functional expression in cultured astrocytes treated with gp120 or cytokines.

**Methods:** Primary cultures of rat astrocytes were incubated (i.e., 6 h, 12 h, 24 h) in the presence of 1.0 nM gp120 (subtype C, strain 96ZM651) or cytokines (i.e., 0.3-0.5 ng/ml and 10 ng/ml, TNF-α, IL-1β, IL-6). Gene and protein expression were determined by RT-PCR and immunoblotting analysis respectively. Mrp-mediated transport activity was evaluated using a fluorescent Mrp substrate (i.e., BCECF). Efflux of GSH/GSSG was investigated at 37ºC in cultured astrocytes grown as monolayers.

**Results:** RT-PCR analysis demonstrated increased Mrp1 mRNA (2.3-fold). Immunoblot analysis showed increased expression of Mrp1 protein expression in astrocyte cultures treated with gp120 (2.2-fold) and TNF-α (2.7-fold). Cellular retention of BCECF was reduced (2.0-fold) in gp120-treated astrocytes, suggesting increased Mrp-mediated transport. Export of GSH and GSSG were enhanced in gp120-triggered cells, which may indicate susceptibility to oxidative stress. Interestingly, iNOS expression was also increased in gp120-treated cultures, further suggesting the enhanced potential for oxidative damage.

**Conclusions:** Gp120 or cytokine treatment can modulate Mrp1 expression in astrocytes. Further studies need to be undertaken to examine the relationship between transporter expression and oxidative stress in this in vitro model system.

**Contact Information:** Patrick Ronaldson, Tel: 416-946-4032, Email: patrick.ronaldson@utoronto.ca

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### INHIBITION OF HIV-1 REPLICATION THROUGH THE USE OF MODIFIED U1SNRNAS

Rade Sajic [1]; Ken Lee [1]; Kengo Asai [1]; Nicole Lund [1]; Darinka Sakac [2]; Don Branch [2]; Chris Upton [3]; Geneve Awong [4]; J.C. Zuniga-Pflucker [4]; Alan Cochrane [1]
1-Department of Medical Genetics and Microbiology, University of Toronto; 2-Department of Medicine, University of Toronto; 3-Department of Biochemistry and Microbiology, University of Victoria; 4-Department of Immunology, University of Toronto

**Plain Language Summary:** The rapid evolutionary rate of HIV-1 has lead to the emergence of multi-drug resistant variants, emphasizing the need for novel inhibitory methods. One such method could be based upon inhibiting viral gene expression through disruption of HIV-1 RNA processing. A means of accomplishing this goal is through use of modified U1snRNA variants that target highly conserved regions of HIV-1. We have demonstrated such U1 derivatives can be used to yield a dramatic (>95%) suppression of HIV gene expression and are currently testing the potential of this approach in virus challenge assays.

**The Challenge:** To determine which of the identified conserved regions of the HIV-1 terminal exon is capable of inhibiting HIV-1 replication when targeted by the modified U1snRNA by preventing viral 3' end formation. To establish a suitable method of administering these modified U1snRNA constructs as a possible HIV-1 therapeutic.

**Our Approach:** To determine the possible HIV-1 regions capable of inhibiting HIV-1 replication when targeted by the modified U1snRNA, multiple sequences where tested. The complementary 10 nucleotide sequences were inserted in the 5' end of the U1snRNA and tested by determining the HIV-1 protein expression levels when cotransfected with HIV-1 virus. Human cancer cell lines stably expressing the modified U1 constructs were either transiently transfected with HIV-1 provirus or infected with HIV-1. Viral protein production was assayed by Western blot. To verify that the effects were specific to HIV-1 and to minimize any off target effects, the modified U1snRNA were further modified to abolish their original ability to form spliceosome assembly complexes. Other techniques include Northern blotting, RNA protection assays, Alkaline Phosphatase assay, and Chloramphenicol Acetyl Transferase assay. To assay the validity of this inhibitory approach as a potential therapeutic, Hematopoetic Stem cell lines were created that stably expressed one of the modified U1snRNAs. This cell line pushed to a T-cell fate, and subsequently tested for inhibition of HIV-1 replication through a viral challenge.

**Key Findings:** Several sequences of the tested constructs displayed substantial HIV-1 protein inhibition when inserted in the U1snRNA construct. Our studies indicate that these modified U1 constructs can be used synergistically to further inhibit the viral protein expression. The spliceosome deficient U1 construct lacking the U1A binding site maintained partial HIV-1 viral inhibitory properties while the spliceosome deficient U1 construct lacking the U1 70K binding site lost all HIV-1 inhibition. Stable cell lines expressing the modified U1 constructs inhibited to a similar extent when challenged transiently. The result on the potential therapeutic assay in the Hematopoetic Stem cell lines is still pending.

**Impact on Policy and Practice:** We have determined several sequences in HIV-1 that when targeted by the modified U1snRNA inhibit viral structural protein expression by as much as 95%. Partial inhibition was maintained when the modified U1snRNA was further modified to lose spliceosome initiating ability making it a strong candidate as a therapeutic agent for HIV-1.

**Contact Information:** Rade Sajic, Tel: 416-978-2500, Email: rade.sajic@utoronto.ca

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### INCUBATION OF JAR PLACENTAL CELLS WITH HYPERGLYCEMIC RAT PLASMA INCREASES ACCUMULATION OF THE P-GLYCOPROTEIN SUBSTRATE SAQUINAVIR

Gregory Anger [1]; Micheline Piquette-Miller[1]
1-Department of Pharmaceutical Sciences, Leslie Dan Faculty of Pharmacy, University of Toronto

**Plain Language Summary:** The primary objective of our OHTN-funded research program is to examine the influence of maternal disease on the expression of anti-HIV drug transporters and to determine how changes affect drug transfer across the placenta. In the present study, our focus is on gestational diabetes as it is a particularly prevalent condition, affecting approximately 5% of all pregnancies, and is known to involve an inflammatory component. My results to date suggest that treating human placental cells with the plasma of diabetic rats can have an impact on their response to the anti-HIV drug saquinavir.

**Objective:** The purpose of this study was to examine the effect that plasma from hyperglycemic rats and various glucose treatments have on accumulation of the P-glycoprotein substrate saquinavir in JAR placental cells.

**Methods:** Hyperglycemia was induced in female rats via subcutaneous streptozotocin injection (45 mg/kg). Blood was collected from these rats, as well as from vehicle-only normoglycemic controls, nine days later to isolate plasma. Confluent cells were incubated with medium containing 10% hyperglycemic or normoglycemic plasma or medium with modified glucose content (increased 2- or 3-fold) for 24 hrs. [$^3$H]-saquinavir accumulation was then determined after 30 min of exposure. Cell viability was confirmed using MTT.

**Results:** Rats injected with streptozotocin became hyperglycemic (>15 mmol/l) within two days. Hyperglycemic and normoglycemic rat plasma had no effect on proliferation. Relative to those untreated and those incubated in normoglycemic plasma, incubation of JAR cells with hyperglycemic plasma resulted in a significant increase in accumulation of [$^3$H]-saquinavir. Increasing the concentration of glucose present in regular medium had no effect on accumulation. A parallel experiment with the P-glycoprotein inhibitor verapamil confirmed that saquinavir accumulation was mediated by P-glycoprotein.

**Conclusions:** Results indicate that hyperglycemic rat plasma but not normoglycemic rat plasma or glucose treatment increases accumulation of the P-glycoprotein substrate saquinavir in JAR placental cells. Thus, constituents in hyperglycemic rat plasma, such as pro-inflammatory cytokines, modulate P-glycoprotein activity in placental cells.

**Contact Information:** Greg Anger, Tel: 416-946-3154, Email: greg.anger@utoronto.ca

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### INNATE FACTORS AS POTENTIAL MICROBICIDES AGAINST HIV-1 IN THE HUMAN GENITAL MUCOSA

Anna Drannik [1]; Xiao-Dan Yao [1]; Jenniffer Newton [1]; Aisha Nazli [1]; Sumiti Jain [1]; Charu Kaushic [1]; Kenneth Rosenthal [1]
1-Centre for Gene Therapeutics, Department of Pathology and Molecular Medicine, McMaster University

**Plain Language Summary:** We are protected against sexually-transmitted infections, in part, by evolutionarily ancient innate immune factors produced in our genital tracts. Since most HIV-1 infections occur by sexual transmission and since women are at increased risk of HIV infection, our goal is to understand the nature, amounts, mechanisms and role of innate factors in protection of the female genital tract against HIV infection. Better understanding of innate defense against HIV in the genital tract should lead to improved microbicides to prevent HIV infection.

**Objective:** Several factors contribute to HIV-1 resistance, including antimicrobials cathelicidin LL-37, SLPI, and TRAPPIN-2/elafin. We aim to characterize the role of LL-37, SLPI and trappin-2/elafin in inhibition of HIV-1 transcytosis using human genital ECs in vitro. Normal levels of expression as well as a correlation between HSV-2/HIV-1 co-infection, genital viral shedding, innate factors and other antiviral mediators will also be determined.

**Methods:** The role of human recombinant LL-37, SLPI and trappin-2/elafin in vitro against HIV-1 will be assessed in the model of transcytosis with human genital ECs (endometrial and cervical transformed cell lines grown in tissue culture inserts). Viral load will be quantitated using an indicator assay and by p24 measurement. The potential of HIV-1 to alter innate immune responses by human genital ECs will be assessed by measuring levels of expression of TLRs using quantitative RT-PCR. Levels of expression of the innate factors in vaginal/cervical washes in healthy controls and single or HSV-2/HIV-1 co-infected subjects will also be assessed using a multiplex cytometric bead array (CBA).

**Results:** Preliminary experiments showed that pretreatment of HEC-1A cells with human recombinant trappin-2/elafin prior to challenge with HSV-2 as well as R5 and X4 HIV-1 viruses resulted in reduced viral shedding, primarily in the apical site, 24h post infection. Lower viral loads were associated with altered levels of IL-8 and TNFα, as well as mRNA expression of TLR1, 3 and 5. We have also developed an in-house ELISA for measuring TRAPPIN-2 that will be adapted for the CBA. Experiments are underway to assess anti-HIV-1 microbicidal capacity of other innate factors.

**Conclusions:** Trappin-2/elafin may have a potential to impact on HSV-2/HIV-1 mucosal transmission across human genial epithelial cells. However, specific mechanisms of action remain to be elucidated.

**Contact Information:** Anna Drannik, Tel: 905-524-1850, Email: drannik@mcmaster.ca

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### MULTI-ANALYTE PROTEIN BEAD ASSAY FOR DETECTION OF HIV ANTIBODIES IN VACCINATED INDIVIDUALS

Bethany M. Henrick [1]; Jennifer Newton [1]; Kenneth Rosenthal [1]
1-Department of Pathology, McMaster University

**Plain Language Summary:** A major challenge to development and testing of mucosal vaccines against HIV is the difficulty in getting large amounts of mucosal secretions for testing. Recent advances have been made in developing tests that are capable of measuring many substances at once in small amounts of samples. These multi-analyte assays or tests are based on the use of small beads that can measure a large number of individual substances in a small amount of sample. Here we describe our progress on developing such an assay to measure antibody responses to a variety of HIV antigens at once in small amounts of mucosal samples.

**Objective:** A major challenge to development and testing of mucosal vaccines against HIV is the difficulty in assessing mucosal immune responses. Here we initiate the development and standardization of a multi-plex assay that quantifies HIV-specific antibodies in both mucosal and systemic samples. This assay allows the quantification of antibodies specific to different epitopes of the virus and quantification of overall immunoglobulin levels of systemic and mucosal samples.

**Methods:** HIV-specific antibodies, namely recombinant 2F5 IgG and IgA, were captured using gp41 peptides previously covalently linked to polystyrene beads. If the antibody was present, it was tagged with fluorescent secondary antibodies specific for the Fc portion of the antibody. These antigen-antibody-antibody complexes were quantified using the mean fluorescence intensities emitted from the secondary fluorescent, either Fluorescein (FITC) a commonly used microscopy dye or R-Phycoerythrin (PE), a commonly used immunofluorescence dye. From these data, standard curves were made with the known concentrations of 2F5 IgG or IgA antibodies.

**Results:** To date, capture beads have been successfully conjugated to virus-specific peptides and anti-human antibodies for human IgG, IgA, and gp41-specific antibodies. Secondary fluorescent indicators for IgG and IgA have successfully been produced using mouse anti-human IgG and IgA specific for the Fc-region of the antibody. These products have been used in experiments of both human mucosal and systemic samples, including vaginal secretions, breast milk, saliva, tears, plasma, and serum. From these experiments, preliminary standard curves have been produced for gp41-specific IgG antibodies in HIV-positive plasma samples and baseline IgG and IgA levels have been quantified for vaginal samples and plasma samples of HIV-negative samples.

**Conclusions:** Conclusion: Results from our lab have been very positive, showing high levels of sensitivity for HIV-specific antibodies and broad-spectrum antibodies. Further experiments of vaginal, breast milk, and serum are required for standardization of this assay.

**Contact Information:** Bethany Henrick, Tel: 905-525-9140 x22494, Email: henricbm@mcmaster.ca

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### MULTI LOW-DOSE MUCOSAL SIVMAC239 CHALLENGE OF CYNOMOLGUS MACAQUES IMMUNIZED WITH "SIMPLIFIED" SIV CONSTRUCTS

David O. Willer [1,2]; Bing Li [1]; Yongjun Guan [1]; Mark A. Luscher [1]; Rick Pilon [3]; Jocelyn Fournier [4]; Mark A. Wainberg [5]; Paul A. Sandstrom [3]; Kelly S. MacDonald [1,2]
1-Division of Clinical Sciences, University of Toronto; 2-Department of Microbiology, Mt. Sinai Hospital; 3-National HIV and Retrovirology Laboratories, Public Health Agency of Canada; 4-Animal Resources Division, Health Products and Food Branch, Public Health Agency of Canada; 5-McGill University AIDS Centre

**Plain Language Summary:** The most promising HIV vaccine approach to inducing sterilizing immunity has been through the use of live attenuated virus vaccines based on monkey (simian) immunodeficiency virus (SIV). In particular, SIV strains engineered with deletions of nef, have afforded the best protection upon challenge with pathogenic SIV. However, the demonstrated potential of nef-deleted SIV strains to revert to full virulence suggests that multiple genetic modifications may be required to assure the safety of such constructs. We have prepared variants of SIV that were designed to replicate poorly in animals, due to deletions within multiple genes. These were administered as a vaccine to cynomolgus macaques. We have investigated the protective efficacy of these "simplified" SIV vaccine vectors in cynomolgus macaques following a multi-low dose intra-rectal challenge with the highly pathogenic SIVmac239 isolate. The use of this specific monkey species and type of challenge was designed to better approximate the genetic diversity and typical dose/challenge/route experienced in the human population.

**Objective:** Here, we are assessing the safety, immunogenicity, and protective efficacy of two novel vaccine candidates (Delta5-CMV and Delta6-CCI), which have been engineered to eliminate all viral accessory genes from SIVmac239, ie. nef, vpr, vpx, vif, tat and rev, yielding what could best be described as a "simplified" retrovirus.

**Methods:** SIV-specific humoral immune responses were assessed throughout the vaccination schedule by western blotting. Cellular immunogenicity was monitored by evaluation of peripheral T-cell responses (via IFN-gamma Elispot assay) following stimulation with peptide pools spanning the entire SIVmac239 genome. The protective efficacy of the different vaccine candidates was determined by quantitative analysis of plasma viral loads and quantitative immunophenotyping of lymphocyte subsets following mucosal challenge.

**Results:** Vaccination induced both humoral and cellular immune responses. A subset of vaccine recipients exhibited marked reduction in peak viral loads, viral load set point, were able to maintain significant levels of peripheral CD4+ T cells, and showed no evidence of clinical symptoms. No evidence of reversion of the viruses to the virulent form was detected in long-term follow up.

**Conclusions:** Although vaccination with "simplified" SIV constructs did not offer sterilizing immunity, vaccination induced both humoral and cellular immune responses which had a significant impact on disease pathogenesis. Our results suggest that genetically attenuated SIV can be used safely as an immunogen without evidence of reversion to the virulent form. Furthermore, we have illustrated the utility of cynomolgus macaques and multi-low dose mucosal challenges in assessing the protective efficacy of SIV vaccine candidates.

**Contact Information:** David Willer, Tel: 416-946-3732, Email: david.willer@utoronto.ca

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### UPREGULATION OF P-GLYCOPROTEIN (P-GP), AN EFFLUX DRUG TRANSPORTER, BY PROTEASE INHIBITORS (PIs) IN A HUMAN BRAIN MICROVESSEL ENDOTHELIAL CELL LINE

Gary N.Y. Chan [1]; Jason A. Zastre [1]; Manisha Ramaswamy [1]; Reina Bendayan[1]
1-Department of Pharmaceutical Sciences, Leslie Dan Faculty of Pharmacy, University of Toronto

**Plain Language Summary:** Atazanavir is currently recommended in ritonavir boosted and unboosted HAART regimens for the treatment of HIV-1 infection. However, little information is known on the effect of atazanavir on drug efflux transporters (i.e., P-gp) expression at the blood-brain barrier (BBB). Previous data have shown the inductive effect of other PIs, in particular ritonavir, on the expression of drug efflux transporters. In addition, many PIs have been shown to be ligands of the nuclear receptor, Pregnane X receptor (PXR), a known regulator of P-gp. Our data suggest that both atazanavir and ritonavir induce P-gp expression and function in an in vitro human BBB model. We hypothesize that the inductive properties of atazanavir on drug efflux transporter expression are mediated through the activity of PXR. Since several PIs are known substrates of P-gp, this may further contribute to limit and restrict CNS penetration of antiretroviral drugs in the brain.

**Objective:** To investigate the effect of atazanavir and ritonavir on the functional expression of P-gp and to examine the role of PXR in an immortalized human brain microvessel endothelial cell line, hCMEC/D3.

**Methods:** Cell viability was assessed in the presence of atazanavir or ritonavir in hCMEC/D3 cells using an MTT assay. Expression of P-gp and hPXR in hCMEC/D3 cells treated with PIs was determined by western blot analysis. To examine functional activity, accumulation of the fluorescent P-gp probe, Rhodamine-6G(R-6G), was assessed in control and treated cells with or without the P-gp inhibitor, PSC-833.

**Results:** Cell viability was over 80% at concentrations ranging from 1 to 10 µM for atazanavir or ritonavir. PXR expression was confirmed by western blot analysis. Treatment of hCMEC/D3 cells for 72h with 5 µM or 10 µM of atazanavir or ritonavir resulted in a 2-fold increase in P-gp expression which in turn translated in a significant reduction in cellular accumulation of R-6G (approximately 2-fold). Furthermore, the P-gp inhibitor, PSC-833, significantly increased R-6G accumulation by 2-fold in treated hCMEC/D3 cells when compared to control.

**Conclusions:** Exposure of atazanavir or ritonavir at clinical therapeutic concentrations resulted in an upregulation of P-gp expression and function in a human brain microvessel endothelial cell line, representative of the BBB. The role of PXR in regulating P-gp expression at the BBB is presently investigated in our laboratory. The inductive properties of PIs on P-gp may contribute to limit CNS penetration of antiretroviral drugs. (Supported by CIHR).

**Contact Information:** Gary Ngai Yin Chan, Tel: 416-946-4032, Email: regulus.chan@utoronto.ca

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### DEVELOPING HIGHLY SENSITIVE IMMUNE ASSAYS TO MEASURE MUCOSAL IMMUNE RESPONSES TO HIV IN THE FEMALE GENITAL TRACT

Duncan Chege [1]; Anuradha Rebbapragada [1]; Sanja Huibner [1]; Charles Wachihi [2]; Joshua Kimani [2]; Blake Ball [3]; Fowke Keith [3]; Walter Jaoko [2]; Francis Plummer [3]; Rupert Kaul [1,2]
1-Clinical Sciences Division, University of Toronto; 2-Department of Medical Microbiology, University of Nairobi, Nairobi, Kenya; 3-Department of Medical Microbiology, University of Manitoba

**Plain Language Summary:** Some individuals remain HIV uninfected despite high levels of exposure to HIV during unprotected sex. Whether immune responses against HIV protect these "highly exposed persistently seronegative" (HEPS) individuals has not been proven, but if they do they should be present at the site of exposure, i.e. the lining of the rectum or genital tract. We aim to measure HIV-specific immune responses in the female genital tract (FGT) of HEPS female sex workers, in order to identify the mucosal immune responses mediating protection. This requires developing sensitive mucosal immune assays to measure changes in FGT cytokine gene expression and cytokine protein production upon activation with HIV proteins.

**The Challenge:** The immune responses described in HEPS women have been weak relative to those seen in HIV infected women, and limited cell numbers are obtained from cervical cytobrush sampling of the FGT. Bacteria naturally present in the FGT make long-term culture of mucosal cells difficult. We aim to develop alternate methods to sensitively measure FGT responses and overcome the limitations inherent in conventional immune assays.

**Our Approach:** To overcome problems of sensitivity and low input cell numbers in mucosal assays using (a) real-time quantitative polymerase chain reaction (qPCR) to measure the accumulation of cytokine gene transcripts, and (b) a chemiluminescent multiplex ELISA to measure secreted cytokine protein from FGT specimens stimulated with HIV antigens. Pilot experiments have been conducted in peripheral blood derived mononuclear cells (PBMCs) to optimize protocols. Small numbers of PBMCs were stimulated with either a pool of HIV peptides spanning the entire HIV genome (GP), media or the super antigen staphylococcal enterotoxin B (SEB). To determine cytokine production kinetics, PBMCs were harvested at hourly intervals (1 to 12 hours post-stimulation) and cytokine gene expression and protein production were assayed. qPCR and multiplex ELISA enabled the simultaneous measurement of gene transcripts and protein levels for up to 12 cytokines.

**Key Findings:** Cytokine gene induction measured by qPCR revealed that cytokine transcripts peaked at 6 hours post-stimulation with HIV-GP. The multiplex ELISA permitted highly sensitive detection of 12 cytokines with a lower limit of detection at 0.5pg/ml. The assays were robust down to an input cell number of 1x105.

**Impact on Policy and Practice:** Based on these promising pilot results, we aim to use these assays to measure mucosal immune responses in HEPS individuals, to better understand the immune correlates of HIV protection.

**Contact Information:** Duncan Chege, Tel: 416-946-7054, Email: duncan.chege@utoronto.ca

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### REGULATION OF P-GLYCOPROTEIN (P-GP) EXPRESSION BY THE MITOGEN-ACTIVATED PROTEIN KINASE (MAPK) PATHWAY IN CULTURED RAT ASTROCYTES TREATED WITH GP120

Patrick Ronaldson [1]; Janica Chan [1]; Christopher Tran [1]; Reina Bendayan [1]
1-Department of Pharmaceutical Sciences, Leslie Dan Faculty of Pharmacy, University of Toronto

**Plain Language Summary:** P-gp is a drug pump involved in exporting anti-HIV drugs from the brain. Our laboratory has observed reduced P-gp levels in astrocytes, a brain cell that can be infected with HIV-1, during exposure to the HIV-1 protein gp120. However, the cellular processes involved in modifying P-gp levels are unknown. Our goal was to investigate cellular processes that may be responsible for changes in P-gp levels. When we treated astrocytes exposed to gp120 with chemicals that interfere with the MAPK pathway, a cell system activated during HIV-1 infection, P-gp levels did not change. In addition, we showed that MAPK enzymes are activated in response to gp120 treatment. These observations suggest that the MAPK system may be involved in modifying P-gp levels during brain HIV-1 infection.

**Objective:** Recently, our laboratory has shown decreased functional expression of P-gp, an ATP-dependent efflux drug transporter involved in limiting brain accumulation of antiretroviral drugs, in cultured rat astrocytes exposed to gp120 or IL-6, a proinflammatory cytokine. However, the intracellular signaling pathways involved in this response have not been elucidated. Studies have shown that cytokines may activate the MAPK pathway, an intracellular system of enzymes known to be involved in regulation of gene expression during pathological conditions. Our goal was to determine the role of the MAPK pathway in the regulation of P-gp expression in gp120-treated cultured rat astrocytes.

**Methods:** Primary cultures of rat astrocytes were incubated (6 h, 24 h) with 1.0 nM gp120 (subtype C, strain 96ZM651) in the presence of MAPK inhibitors [i.e., MEK1 inhibitor PD98059 (50 μM), p38 MAPK inhibitor SB203580 (20 μM), c-Jun N-terminal kinase inhibitor SP600125 (20 μM)]. Cell lysates were analyzed for total and phosphorylated MAPK enzymes (i.e., ERK1/2, p38 MAPK, JNK1α/β) and for P-gp using immunoblot analysis.

**Results:** In primary cultures of rat astrocytes triggered with gp120, immunoblot analysis showed decreased P-gp expression (4.7-fold). In contrast, P-gp protein expression was not altered in cultured astrocytes exposed to gp120 and MAPK inhibitors (i.e., PD98059, SB203580, SP600125). Expression of phosphorylated ERK1/2 was increased after 6 h gp120 treatment but was decreased after 24 h gp120 exposure relative to untreated controls.

**Conclusions:** These data suggest that the MAPK pathway may be involved in the regulation of P-gp expression during HIVE-associated immunological responses. Further studies are required to confirm the signaling molecules involved in cytokine release and in the alteration of P-gp expression.

**Contact Information:** Patrick Ronaldson, Tel: 416-946-4032, Email: patrick.ronaldson@utoronto.ca

## 213

### IMMUNIZATION BY INTRANASAL AND SUBCUTANEOUS ROUTES, UNDER THE INFLUENCE OF ESTRADIOL, PROTECTS AGAINST GENITAL HSV-2 INFECTION

Sudha Bhavanam [1]; Amy Gillgrass [1]; Charu Kaushic [1]
1-Center for Gene Therapy, Dept of Pathology and Molecular Medicine, McMaster University

**Plain Language Summary:** Over past two decades, there have been numerous efforts to develop vaccines to treat or prevent HSV-2 infection. An important goal of vaccination against sexually transmitted infections (STIs) is to induce immunity in the female reproductive tract. Hormones play an important role in the induction of protective immune responses. In this study we examined whether different routes of immunization would provide equivalent protection under different hormonal conditions.

**Objective:** To examine the effect of hormones on systemic vs. mucosal route of immunization against HSV-2.

**Methods:** C57BL/6 mice were overiectomized and mice were treated with estradiol (E) progesterone (P) or placebo pellets for 21 days. The groups were than immunized either once by intranasal (IN) route on day 7 of hormone treatment or three times by subcutaneous (SC) route on day 7, 14 and day 21 with attenuated HSV-2 (TK-). Four weeks after immunization, mice were challenged intravaginally (IVAG) with HSV-2. Mice were monitored for pathology, survival and vaginal washes were collected to detect the viral load. IgG and IgA were detected in vaginal samples and serum samples post immunization and HSV-2 challenge by ELISA.

**Results:** We compared intranasal (IN) and subcutaneous (SC) routes of immunization and the effect of reproductive hormones on immune responses against HSV-2. Mice immunized IN had 83% survival in E, following challenge. P group had 50% survival and placebo group had 66% survival. SC immunized group had 100% survival in E; P treated mice had 83% and placebo group had 66% survival. Highest survival was seen in E-treated groups by both routes of immunization compared to P-treatment. Even though the overall percent survival in SC immunized mice was higher when compared to IN immunized group, the pathology scores in SC immunized group were higher and longer lasting compared to IN immunized mice. HSV-2 specific IgG antibodies in the vaginal washes and serum samples after challenge correlated closely with protection.

**Conclusions:** The results so far indicate that immunization under the influence of estradiol leads to clearance of genital HSV-2 infection by both intranasal and subcutaneous immunization. Progesterone treated mice had partial protection. Both routes of immunizations are feasible for induction of anti-viral immune response in the reproductive tract. Vaccine strategies must take into account the effect of sex hormones on immune responses.

**Contact Information:** Sudha Bhavanam, Tel: 905-525-9140 x22589, Email: bhavans@mcmaster.ca

## 214

### RAPID, HIGH-THROUGHPUT HIV-1 SUBTYPING USING A HIGH-RESOLUTION MELTING ASSAY

Hezhao Ji [1]; Harriet Merks [1]; Nathalie Masse [1]; Isabelle Joanisse[1]; Paul Sandstrom[1]; James Brooks [1]
1-National HIV & Retrovirology Laboratories, Public Health Agency of Canada

**Plain Language Summary:** HIV-1 is genetically diverse with multiple clades/subtypes identified globally. Different HIV-1 subtypes have been associated with varied rates of disease progression and responses to antiretroviral treatment regimens. Determination of HIV-1 subtype provides public health with insight into the patterns of HIV transmission and may provide important clinical information. Currently, genotypic testing of the viral RNA from infected patients is used to define the subtype. This analysis is expensive and requires both significant laboratory infrastructure and highly trained personnel. In this study, we applied high-resolution melting (HRM) analysis, to determine HIV-1 subtype. Promising results derived from this project demonstrate that HRM may have application as a simplified, rapid and cost-effective tool in HIV subtype surveillance.

**The Challenge:** The compact and efficient HIV genome necessitates complex, expensive and time-consuming laboratory procedures to resolve HIV-1 subtype using molecular methods. Cost-effective, simple molecular tests that can be performed in basic laboratories would improve subtype surveillance.

**Our Approach:** We employed HRM to examine its applicability to HIV-1 subtype determination. HRM characterizes the dissociation of double stranded DNA ("melt") with extremely high resolution. Employing inexpensive intercalating dyes such as SYTO 9, HRM obviates the need for costly fluorescence-labeled oligonucleotide probes. In a simple, rapid, closed-tubed method, using specific primers in an HRM thermocycling system, we can detect sufficient differences in melting temperature to resolve HIV-1 subtype.

**Key Findings:** Preliminary results demonstrate that HRM methodology can rapidly and cost-effectively resolve the main endemic HIV subtypes in Canada such as clades B, A1 and C. Currently, the assay is being refined to identify further HIV-1 subtypes.

**Impact on Policy and Practice:** A rapid and cost-effective tool is needed for population-based HIV subtype surveillance. The HRM-based HIV subtyping method presented here has great potential to simplify aspects of the Canadian HIV-1 surveillance program. Furthermore, by reducing the complexities, laboratory requirements and costs associated with traditional HIV subtype determination, this methodology may find application in resource poor countries.

**Contact Information:** Hezhao Ji, Tel: 613-952-9446, Email: hezhao_ji@phac-aspc.gc.ca

## Immunology

### 215

**GENERATION OF FUNCTIONAL HUMAN T CELLS DERIVED IN VITRO FROM HEMATOPOIETIC STEM CELLS**

Geneve Awong [1,2]; Ross La Motte-Mohs [1,2]; Juan Carlos Zúñiga-Pflücker [1,2]
1-Department of Immunology, University of Toronto; 2-Sunnybrook Health Sciences Centre

**Plain Language Summary:** T lymphocytes are a class of white blood cells that undergo differentiation within the unique microenvironment of the thymus. CD8+ T cells kill virally infected cells, while CD4+ T cells play a role in augmenting the effector function of CD8+ T cells. A hallmark feature of infection with HIV and AIDS is the chronic decline in the number of CD4 helper T cells. Our lab has generated a stromal cell line (OP9-DL1) that upon coculture with umbilical cord-blood hematopoietic stem cells (HSCs) supports the generation of functional CD4+ and CD8+ human T cells. Here, we characterize the development and functional capacity of these in vitro derived T cells. In addition, we have demonstrated that normal T cell development is observed from genetically modified HSCs expressing an HIV inhibitor and are testing whether these cells display decreased susceptibility to infection.

**Objective:** This investigation uses the OP9-DL1 coculture system to assess the phenotypic, molecular and functional status of human T cells derived in vitro from a defined source of HSCs.

**Methods:** Human cord-blood samples were obtained from consenting mothers following delivery at Women's College Hospital. Human CD34+CD38- stem cells were sorted from the blood and cocultured on stromal cells. Cocultures were disaggregated at the various time-points and cells were either stained with antibodies for flow cytometry or RNA was isolated and reverse-transcribed into cDNA for PCR. To test functionality, T cells were stimulated for 5 days and proliferation measured by CFSE dilution. For HSC genetic modification, constructs were introduced into HSCs via lentiviral transduction and sorted 2 days later based on GFP positivity.

**Results:** We observed hematopoietic stem cell differentiation toward the T cell lineage as characterized by the acquisition of cell-surface markers CD7, CD1a, CD5, CD4 and CD8. At the molecular level, T cell associated genes were induced in OP9-DL1 cocultures. These genes include Gata-3, Deltex-1 and Rag-1. In vitro derived CD4+ and CD8+ T cells are mature and functional as they upregulate activation markers and proliferate following stimulation. In addition, HSCs transduced to express an HIV inhibitory construct have been generated and are able to undergo normal phenotypic development.

**Conclusions:** The OP9-DL1 coculture system efficiently initiates and supports the differentiation of functional T cells from human stem cells. We show that T cell specification and commitment events were induced at both the phenotypic and molecular level, in addition to proliferation at the functional level. This system has an important potential as it provides the foundation for a large supply of human T lymphocyte progenitors, which could be used in the clinical setting for immune-reconstitution of HIV-infected individuals.

**Contact Information:** Geneve Awong, Tel: 416-480-6100 x7340, Email: gawong@sri.utoronto.ca

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**INFLUENCE OF ANTIGEN AND COMMON GAMMA CHAIN CYTOKINES ON CD8+ T CELL PROLIFERATION AND FUNCTION**

Alison M. O'Connor [1]; Gerry W. Greco [1]; Angela M. Crawley [1,2]; Jonathan B. Angel [1,2,3]
1-University of Ottawa-Department of Biochemistry, Microbiology, and Immunology; 2-Ottawa Health Research Institute; 3-Division of Infectious Diseases-Ottawa Hospital General Campus

**Plain Language Summary:** Progressive HIV infection is associated with the loss of CD8+ T cell function, and decreased expression of IL-7Rα (CD127), which is important for T cell development and proliferation. This may contribute to CD8+ T cell impairment during HIV infection. Common gamma chain cytokines, such as IL-2, -4, and -15, have differential effects on CD8+ T cell development and functional responses, and these effects may vary due to expression of CD127. CD127 expression on CD8+ T cells may be indicative of functional cell subsets.

**Objective:** To determine the effects of IL-2, -4, and -15 on antigen-specific CD8+ T cell proliferation and function in the context of CD127 expression

**Methods:** Blood monocyte-derived dendritic cells were pulsed with a peptide pool (EBV, CMV, influenza) and co-cultured with autologous CD8+127+ or CD8+127- T cells in the presence or absence of IL-2, -4, or -15. After seven days of culture, cell division (CFSE) and function (IFN-γ, IL-2) were analyzed by flow cytometry. Naïve, central memory, effector memory, and terminally differentiated effector memory T cell subsets were identified on the basis of CD45RA and CCR7 expression.

**Results:** The presence of common gamma chain cytokines IL-2 and -15 increased the relative number of CFSElo cells compared to antigen alone. Proliferation was greater in the CD8+CD127- T cells compared to CD8+CD127- T cells. Effector memory and terminally differentiated memory cells proliferated to a greater degree compared to naïve and central memory cells, indicating a more rapid response to antigen by these CD8+ T cell subsets.

**Conclusions:** Interleukin-2 and -15 induce proliferation of all CD8+ T cell subsets in response to antigen, suggesting a role for these cytokines in CD8+ T cell function. Effector memory and terminally differentiated memory CD8+ T cells prior exposure to antigen previously may explain the observed increased proliferative response from these subtypes. These results further our understanding of CD8+ T cell function and may be relevant to HIV pathogenesis.

**Contact Information:** Alison O'Connor, Tel: 613-737-8160, Email: alioconnor@ohri.ca

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### VPR-MEDIATED SUPRESSION OF IL-12 MAY BE DUE TO ALTERED CD14, TLR4 AND GLUCOCORTICOID RECEPTOR EXPRESSION

Fiona Frappier [1,2]; Jonathan Angel [1,2,3]
1-University of Ottawa; 2-Ottawa Health Research Institute; 3-General Hospital

**Plain Language Summary:** The goal of this project is to outline new potential therapeutic targets to improve the health and longevity of people with HIV infection. To achieve this goal, we are characterizing the signals required for the production of IL-12, a critical signaling molecule of the immune system. IL-12 is a prime candidate to achieve our goal, since its production is impaired in people with AIDS leading to increased susceptibility to additional infections. The project focuses on the HIV protein Vpr's ablility to decrease IL-12 production by affecting a stress hormone receptor (the glucocorticoid receptor). Understanding the ways HIV decreases IL-12 production will enhance our understanding of immune suppression.

**Objective:** The inhibition of IL-12 is an important mechanism of HIV mediated immune dysfunction. The HIV accessory protein, Vpr has been shown to act as a potent co-activator of the host glucocorticoid receptor (GR). Broadly our objective is to characterize the cellular mechanism by which HIV and/or Vpr utilizes the glucocorticoid receptor to inhibit IL-12 production. Our objective in this study is to determine if Vpr alters IL-12 p40 protein or any of the upstream CD14, TLR4 and the GR expression.

**Methods:** Peripheral blood mononuclear cells were cultured with a Vpr peptide fragment composed of amino acid 52 to 96 which encompasses the GR binding motif between amino acids 64-68. The GR, TLR4 and CD14 receptor expression was measured on monocytes cultured in PBMCs by flow cytometry. IL-12 p40 protein in supernatants was assessed by ELISA. Sample conditions that altered expression were tested again in the presence or absence of the GR inhibitor Ru486 to determine which effects are GR-mediated.

**Results:** We demonstrate the inhibitory effects of the truncated Vpr peptide (0.005 uM) on IL-12 p40. Inhibiting the GR pathway with RU486 prevents the Vpr mediated inhibition of IL-12 p40 in PBMCs. Vpr peptide induces a significant decrease of CD14 and TLR4 which are critical upstream signaling molecules of the IL-12 p40. Vpr peptide also leads to an important increase in GR expression.

**Conclusions:** Our observations explain in part the ability of HIV to decrease IL-12 p40 through the HIV protein Vpr. The increased expression of GR by Vpr may be creating a positive feedback loop leading to further inhibition of IL-12 p40. In the absence of IL-12, the cell-mediated immune response to the invading pathogen is deficient. Therefore, understanding the regulation of IL-12 production and the mechanism of HIV-inhibition is of great therapeutic interest.

**Contact Information:** Fiona Frappier, Tel: 613-737-8160, Email: ffrappier@ohri.ca

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### IL-7 DECREASES IL-7 RECEPTOR α (CD127) EXPRESSION AND INDUCES THE SHEDDING OF CD127 BY HUMAN CD8+ T-CELLS

Agatha Vranjkovic [1,2]; A. Crawley [1,2]; K. Gee [1,2]; A. Kumar [2,3]; J. Angel [1,2,4]
1-Ottawa Health Research Institute; 2-Department of Biochemistry, Microbiology and Immunology, University of Ottawa; 3-Division of Virology and Molecular Immunology, Children's Hospital of Eastern Ontario Research Institute; 4-Division of Infectious Diseases, Ottawa Hospital-General Campus

**Plain Language Summary:** Interleukin (IL)-7 receptor α (CD127) signalling is essential for T cell development and regulation of naïve and memory T cell homeostatis. Fewer CD8+ T cells from HIV-infected patients express CD127 compared to healthy individuals, suggesting that specific host and/or viral factors regulate IL-7 receptor expression.

**Objective:** To determine which host or viral factors may be responsible for the downregulation of CD127 observed on CD8+ T cells in HIV infection and the mechanism(s) thereof.

**Methods:** Factors relevant to HIV infection that could potentially decrease CD127 expression on human CD8+ T cells and the mechanisms by which this occurs were therefore evaluated. CD127 expression was evaluated by flow cytometry, semi-quantitative and quantitative PCR, microscopy and Western blotting of cell supernatants and human plasma.

**Results:** Interleukin-7, but not HIV gp120, IL-1β, IL-6, IL-10, IL-13, TGFβ or TNFα, reduced CD127 surface expression and did so without altering the expression of mRNA encoding membrane-associated CD127. Furthermore, IL-7 did not increase the amount of CD127 detected within the cytoplasm of CD8+ T-cells. Interestingly, culturing CD8+ T cells with IL-7 increased the amount of CD127 detected in the cell supernatants, suggesting that IL-7 induces shedding of CD127. In addition, increased levels of CD127 were observed in the plasma of HIV+ compared to HIV- individuals providing clinical significance to the in vitro findings. Naive CD8+ T-cells are more sensitive to IL-7 mediated downregulation of CD127, suggesting that these effects may have particular significance early in T-cell life cycle.

**Conclusions:** Since CD127 downregulation may be a contributor to HIV-associated T-cell dysfunction, such as impaired CTL, these findings may provide valuable insights into the development of novel immune based therapies for patients infected with HIV.

**Contact Information:** Agatha Vranjkovic, Tel: 613-737-8160, Email: akomsic@ohri.ca

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### THE HIV TAT PROTEIN MAINTAINS SUPPRESSION OF THE INTERLEUKIN-7 RECEPTOR ON CD8 T-CELLS ISOLATED FROM HIV+ PATIENTS

Elliott Faller [1,2]; Mark McVey [2]; Paul MacPherson [1,2,3]
1-University of Ottawa, Faculty of Medicine, Department of Microbiology/immunology; 2-Ottawa Health Research Institute; 3-Division of Infectious Diseases, Ottawa Hospital General Campus

**Plain Language Summary:** Expression of the IL-7 receptor α- chain (CD127) is decreased on CD8 T-cells in HIV infected patients and recovers in those receiving antiretroviral therapy with sustained viral suppression. We have recently shown soluble HIV Tat protein down regulates CD127 on the surface of CD8 T-cells isolated from healthy volunteers and that this down regulation requires the continual presence of Tat. We show here that low CD127 expression on CD8 T-cells isolated from HIV+ individuals also recovers ex vivo to near normal levels when CD8 T-cells are maintained in fresh media and that this recovery can be suppressed by Tat.

**Objective:** To determine the effect of HIV Tat protein on CD127 expression on CD8 T-cells isolated from HIV+ patients.

**Methods:** CD8 T-cells were isolated from HIV + patients and incubated in media alone or with Tat protein as indicated. Surface CD127 expression was measured by flow cytometry.

**Results:** Low CD127 expression on CD8 T cells isolated from HIV+ patients recovers to near normal levels when CD8 T cells are isolated and cultured in media. Recovery of CD127 expression was completely inhibited by the addition of HIV Tat protein to the culture media.

**Conclusions:** This study provides evidence that soluble factors are responsible for low CD127 expression on circulating CD8 T cells in HIV+ individuals and further supports the role of Tat in suppression of this receptor essential to CD8 T cells proliferation and function.

**Contact Information:** Elliott Faller, Tel: 613-864-3414, Email: efaller@ohri.ca

## 220

### GP120 BINDING TO A GLYCOLIPID CO-RECEPTOR, GB3: LIPID RAFTS, ISOFORM DEPENDENCY AND CHOLESTEROL REQUIREMENT

Adam Manis [1,2]; Clifford Lingwood [1,2,3]
1-Molecular Structure and Function, The Hospital For Sick Children; 2-Laboratory Medicine and Pathobiology, University of Toronto; 3-Department of Biochemistry, University of Toronto

**Plain Language Summary:** Host cell glycolipids can function as cell co-receptors in HIV infection. One such glycolipid is globotriaosyl ceramide, Gb3. We have found that binding of HIV gp120 to Gb3 requires cholesterol, and is modulated by the fatty acid content of Gb3. The possibility that adamantylGb3, a soluble, semi-synthetic derivative of Gb3 previously shown to inhibit HIV infection and gp160-mediated fusion, inhibits at the level of viral-host cell binding, is also under investigation.

**The Challenge:** To determine what role the binding of gp120 to Gb3 plays in HIV infection. Gb3 is found in cholesterol enriched lipid rafts in target cells. Such rafts are required for infection. We have attempted to mimic such rafts in vitro, and determine the Gb3/cholesterol format which promotes gp120 binding. This assay allows the assessment of other factors, e.g. solubleCD4, different strains of HIV, and adamantylGb3, on gp120-Gb3 binding.

**Our Approach:** The model used simulates lipid rafts. A 2:1 ratio of Gb3 to cholesterol is dried down and re-suspended in a 1% Triton-containing buffer, vortexed, sonicated and heated in a water bath in order to form Gb3/cholesterol vesicles. The vesicles are overlaid with sucrose containing gp120 and a sucrose gradient (35%-5%), and ultracentrifuged. The location of gp120 within the gradient (indicating binding) is detected immunologically. Alternatively, gp120 is not included in the gradient and the different fractions are later incubated with a gp120 to monitor binding.

**Key Findings:** While most of the Gb3 is within the theoretical raft fraction (30/5% sucrose interface), gp120 binding occurs only at the top of the gradient where only a minor fraction of the Gb3 migrates. Gb4 is not bound. Gb3 fatty acid content modulates binding of gp120. The C16, C22, and C24 length fatty acid containing isoforms all bind gp120 while no binding is seen with the C18 and C20 analogues (a similar binding profile is seen for the E.coli verotoxin). Gp120 binding requires cholesterol as no binding was detected to Gb3 alone. Direct gp120 binding to the unseparated Gb3/cholesterol vesicles bound to nitrocellulose will allow for quantitation of potential adamantylGb3 inhibition.

**Impact on Policy and Practice:** These studies should contribute both to a better understanding of HIV entry into host cells as well as further characterizing the mechanism by which adamantylGb3, currently under investigation as a possible anti-HIV microbicide, inhibits viral entry into cells.

**Contact Information:** Adam Manis, Tel: 416-875-8230, Email: adam.manis@utoronto.ca

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### REGULATION OF CD127 GENE EXPRESSION IN CD8 T-CELLS

Juzer Kakal [1,2]; Scott Sudgen [1,2]; Elliott Faller [1,2]; Ritesh Kumar [3]; Paul MacPherson [1,2,3,4]
1-University of Ottawa - Department of Biochemistry, Microbiology and Immunology; 2-Ottawa Health Research Institute - Department of Molecular Medicine; 3-University of Ottawa – Faculty of Medicine; 4-The Ottawa Hospital - Division of Infectious Diseases

**Plain Language Summary:** Interleukin (IL)-7 plays a key role in peripheral immune homeostasis and is essential to CD8 T-cell survival, proliferation and cytolytic activity. Factors regulating expression of the IL-7 receptor throughout the CD8 T-cell life-span have not been fully characterized but IL-7 has been shown to down regulate the IL-7 receptor α-chain (CD127) at the cell surface. Here we show IL-7 suppresses CD127 gene transcription and that the CD127 gene promoter is contained within the first 3000 bp upstream of the TATA box.

**Objective:** To identify the minimal CD127 gene promoter in CD8 T-cells.

**Methods:** CD8 T-cells were isolated from healthy HIV-negative volunteers and incubated in RPMI 1640 plus 20% FCS either alone or with IL-7 (10 ng/ml) for 24 hours. Total RNA was harvested and CD127 mRNA transcripts were quantified using real-time PCR normalizing to RPS18. Transcripts encoding all forms of CD127 were measured using a forward primer spanning the exon 2/3 boundary while mRNA encoding the secreted isoform of CD127 where exon 6 is spliced out were quantified using a forward primer spanning the exon 5/7 boundary. To identify the gene promoter, DNA fragments from the TATA box to -100, -262, -626, -1200 and -2900 respectively were cloned from genomic DNA isolated from Jurkat T-cells and placed upstream of a firefly luciferase reporter gene. Resting primary CD8 T-cells were transfected using the nucleofection protocol and luciferase activity was quantified.

**Results:** IL-7 induced a 65% decline in the level of total CD127 transcripts in CD8 T-cells compared to cells maintained in media alone. Since IL-7 had no effect on mRNA stability, it appears CD127 down regulation by IL-7 occurs at the level of transcription initiation. We also found decreased levels of transcripts encoding the secreted isoform of CD127 in the presence of IL-7 suggesting that down regulation did not occur as a result of differential splicing. The promoter sequences necessary for CD127 gene expression in resting CD8 T-cells are contained within the first 2900 bp upstream of the TATA box. While promoter fragments extending from the transcription initiation site as far upstream as -1200 bp provided ≤ 4 fold expression above empty vector, including sequences to -2900 bp provided luciferase activity 12.5 fold above background.

**Conclusions:** IL-7 down regulates CD127 gene expression at the level of transcription initiation. We next plan to carry out a mutational analysis of the CD127 gene promoter to identify IL-7 responsive elements.

**Contact Information:** Juzer Kakal, Tel: 613-737-8673, Email: jkakal@ohri.ca

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### ARE SOME CTL EPITOPES VIRAL DECOYS? VIRAL PRESSURES INFLUENCING IMMUNODOMINANT CTL EPITOPE SEQUENCE EVOLUTION IN HIV

Natasha M. Christie [1]; David O. Willer [2,3]; Michael Lobritz [4]; Mark A. Luscher [2]; Eric J. Arts [4]; Kelly S. MacDonald [2,3]
1-Department of Immunology, University of Toronto; 2-Division of Clinical Sciences, University of Toronto; 3-Department of Microbiology, Mt. Sinai Hospital; 4-Department of Molecular Biology and Microbiology, Case Western Reserve University, Cleveland, OH, USA

**Plain Language Summary:** Positive selection of mutations within highly targeted cytotoxic T-lymphocyte (CTL) epitopes during HIV replication is well documented. However, this accumulation of immune evasion type mutations does not appear to affect all epitopes equally. The diversity in mutation rate among immunodominant epitopes is widely attributed to the differential viral fitness requirements of epitope regions, but may also be the consequence of a compromised CTL response that is unable to place appropriate negative pressure on certain widely targeted epitopes.

**Objective:** This work is aimed at determining the extent to which viral fitness requirements dictate sequence conservation in the HLA-A2 restricted immunodominant epitope SLYNTVATL (SL9).

**Methods:** HIV clones incorporating synonymous or non-synonymous mutations throughout the SL9 epitope region have been constructed in order to determine their effect on viral replication and fitness. Due to the congenic nature of the viral constructs created, any infectivity or growth defects could be traced directly to the changes in the epitope sequence in question. Individual viral viability and infectivity was determined by mono-infection assays in T-cell line culture. Furthermore, dual-infection competition assays were performed in peripheral blood mononuclear cell (PBMC) culture to assess relative fitness of the viral mutants with respect to the original SL9 sequence.

**Results:** Interestingly, constructs recapitulating SL9 variants seen in vivo showed markedly little effect on viral replication, as did conservative non-synonymous mutations targeting the immunologically relevant residues of the epitope. However, mutations targeting the terminal leucine residue of the epitope indicate a high level of sequence restriction at this MHC anchor point, as even conservative mutations negatively affected viral replication.

**Conclusions:** Importantly, although certain residues of the epitope are constrained, there are SL9 variants that are well tolerated virologically that fail to arise in vivo, potentially indicating that the SL9-directed immune response is not capable of placing strong selective pressure on this sequence. The identification of specific CTL epitopes which induce immunodominant but non-selective, and hence non-protective immune responses is key to understanding viral pathogenesis and vaccine design.

**Contact Information:** Natasha Christie, Tel: 416-978-1605, Email: natasha.christie@utoronto.ca

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### REGULATION OF RESISTANCE TO HIV-VPR INDUCED APOPTOSIS IN MONOCYTIC CELLS

S. Mishra [1]; J.P. Mishra [1]; A. Kumar [1,2,3]
1-Biochemistry, Microbiology and Immunology Department, CHEO, University of Ottawa,; 2-Pathology and Laboratory Medicine Department, CHEO, University of Ottawa; 3-Infectious Disease & Vaccine Research Centre, Research Institute, CHEO, University of Ottawa

**Plain Language Summary:** HIV infects many types of human blood cells including monocytes. Unlike other blood cells which undergo apoptosis following infection, monocytes are able to survive and serve as a continuous reservoir of virus particles. Therefore, we need to understand the fundamental mechanisms involved in this process so that we can formulate effective therapies. It is believed that the pro-inflammatory cytokine, TNF-α which is known to enhance HIV replication may be a key to protect monocytic cells from the cytopathic effects of HIV. In this study, we investigated the signaling pathways involved in HIV-Vpr induced apoptosis and the resistance conferred by TNF-α in monocytic cells. We showed that JNK MAPK is involved in inducing HIV-Vpr mediated apoptosis in monocytes and calcium signaling pathway specifically CAMKII is accountable for conferring protection to Vpr induced apoptosis.

**Objective:** To study the molecular mechanisms involved in inducing resistance to HIV-Vpr mediated apoptosis in monocytes/macrophages.

**Methods:** We have used a synthetic HIV-Vpr peptide to induce apoptosis. LPS and TNF-α are used to induce protection against apoptosis. Apoptosis was measured by Annexin/PI staining and intracellular PI staining. Various MAPK inhibitors, calcium inhibitors, and stealth RNAs are used to assess the involvement of different pathways in the above mentioned process.

**Results:** First of all, we demonstrated that Vpr52-96 induced apoptosis in monocytes. Further, we showed that Vpr52-96 peptide induced phosphorylation of all the three p38, ERK and JNK MAPKs, however, pretreatment of cells with JNK specific inhibitor SP600125 significantly reversed the Vpr52-96-induced apoptosis in a dose dependent manner. We confirmed our observation by stealth siRNA specific for JNK1 and JNK2 to knockdown endogenous and Vpr52-96 induced JNK activation. We also showed that prior stimulation with either LPS or TNF-α inhibited Vpr52-96-induced apoptosis. Further, we demonstrated that LPS/TNF-α mediated resistance is regulated by induction of c-IAP2 through NFκB by activation of CAMKII. However, pretreatment with Vpr followed by LPS or TNF-α stimulation no longer gave protection to Vpr induced apoptosis. Taken together, our results suggest that the c-IAP2 gene plays a critical role in LPS and TNF-α-induced resistance to HIV-Vpr-mediated apoptosis in human monocytic cells.

**Conclusions:** Since the calcium/CAMKII pathway is involved in LPS/TNF-α induced resistance to Vpr mediated apoptosis, strategies based on manipulation of these molecules, which would suppress c-IAP2 induction may be useful in clearing virus reservoirs in monocytes.

**Contact Information:** Sasmita Mishra, Tel: 613-737-7600 x3919, Email: sasmishra@hotmail.com

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### PI3K AND P38 MAPK DIFFERENTIALLY REGULATE EXPRESSION OF IL-12 FAMILY CYTOKINES (IL-23 AND IL-27) IN LPS-INDUCED HUMAN MONOCYTIC CELLS

Ali Akbar Rahim Rahimi [1]; Maria Blahoianu [1]; Niranjala Gajanayaka [3]; Jyoti Mishra [1]; Jonathan B. Angel [1,4]; Ashok Kumar [1,2,3]
1-Department of Biochemistry, Microbiology and Immunology, University of Ottawa; 2-Department of Pathology and Laboratory Medicine, University of Ottawa; 3-Division of Virology and Molecular Immunology, Research Institute, CHEO; 4-Ottawa Health Research Institute and the Division of Infectious Diseases, Ottawa Hospital, University of Ottawa

**Plain Language Summary:** Interleukin (IL)-12 has been well recognized as the cytokine that plays role as a bridge between innate and adaptive immunity, and with discovery of IL-23 and IL-27 as cytokines related to IL-12, there has been a concerted effort to understand the relationship between these cytokines. IL-12 family cytokines are early products of activated monocytes/macrophages and dendritic cells and promote differentiation and function of CD4+ T helper cells leading to cell mediated immune response (CMIR).

**Objective:** In this study, we investigated the IL-27p28, IL-27EBI3, IL-12/IL-23p40 and IL-23p19 regulation at mRNA and protein production level in human primary monocytes and THP-1 cells as model systems.

**Methods:** Regulation of IL-12, IL-23 and IL-27 in human monocytic cells was analyzed by quantitative RT-PCR analysis, and ELISA. The siRNA technology was used to confirm the involvement of signaling pathways.

**Results:** We defined that priming the cells with IFN-γ is necessary to response to LPS stimulation in primary monocytes in vitro. Also we showed the distinct signaling mechanisms that regulate the LPS-mediated induction of IL-27 and IL-23 in human monocytic cells. Using specific pharmacological inhibitors and siRNAs, our findings indicate that LPS-stimulated IL-27p28 and IL-27EBI3 production was dependent on the PI3K and p38 MAPK-mediated pathways but LPS-induced IL-23 regulation was not positively regulated by these pathways.

**Conclusions:** The approaches directed at understanding Th1 cytokines regulation by LPS and IFN-γ, separately and synergistically, may be helpful in devising novel strategies to enhance CMIR and facilitate immune reconstitution and potentially eliminate intracellular microorganisms from the body.

**Contact Information:** Ashok Kumar, Tel: 613-737-7600 x3920, Email: akumar@uottawa.ca

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### REDUCED IL-7RA EXPRESSION IN CD8+ CYTOTOXIC T LYMPHOCYTES FROM HIV+ PATIENTS IS ASSOCIATED WITH THE TRANSCRIPTIONAL REPRESSOR GFI-1 AND IMPAIRED STAT ACTIVATION IN RESPONSE TO IL-7 BUT NOT IL-2, IL-15, IL-4, AND IL-10

Anita Benoit [1,4]; Danylo Sirskyj [1,4]; Khaled Abdkader [1,4]; Abdulkarim Alhetheel [1,4]; Nadia Sant [1,4]; Jonathan Angel [4,5]; Ashok Kumar [1,2,3,4]; Francisco Diaz-Mitoma [1,2,3,4]; Marko Kryworuchko [1,2,3,4]
1-Infectious Disease and Vaccine Research Centre, CHEO - Research Institute; 2-Division of Virology, CHEO; 3-Department of Pathology and Laboratory Medicine, University of Ottawa; 4-Department of Biochemistry, Microbiology and Immunology, University of Ottawa; 5-Division of Infectious Diseases, Ottawa Hospital - General Campus

**Plain Language Summary:** Cytotoxic T lymphocytes (CTL) are immune cells that kill virus-infected cells and are critical in the control of HIV replication. However, CTLs from HIV+ patients are unable to clear HIV infection and eventually become functionally impaired and more susceptible to cell death, themselves. The maintenance of these cells requires that they respond properly to growth and regulatory factors of the immune system called cytokines. We studied whether the impairment in these cells was related to alterations in their capacity to respond to signals from cytokines and provide insights into the mechanism by which this may occur.

**Objective:** Studies in chronically-infected HIV+ patients with high virus load have described an increased proportion of Interleukin-7 receptor α low-expressing (IL-7Rα low) effector-like CTLs. Since cytokine signaling through the Signal Transducers and Activators of Transcription (STAT) is essential for CTL homeostasis, we hypothesized that defects in this signaling pathway may be involved in the generation of these cells and elaborated the following study objectives. 1) Evaluate the capacity of IL-7Rα low and IL-7Rα high CTLs from chronically-infected HIV+ patients to activate STAT signaling in response to cytokines critical in CTL homeostasis; 2) Investigate the potential molecular mechanism responsible for IL-7Rα downregulation in patient CTLs.

**Methods:** Chronically-infected HIV+ adults on antiretroviral therapy (ART) and those not undergoing ART for greater than 6 months were recruited into the study. Flow cytometry and quantitative real time PCR (qRT-PCR) experiments were conducted on patient peripheral blood-derived CTLs.

**Results:** IL-7 stimulation failed to activate STAT5 in a substantial proportion of HIV+ patient CTLs. This correlated with a reduction in both IL-7Rα surface protein and mRNA expression, and increased plasma viral load. Interestingly, IL-7Rα low CTLs appeared to be fully capable of recruiting the STAT pathway in response to the other cytokines tested (IL-2, IL-4, IL-10, and IL-15). QRT-PCR experiments showed that expression of the transcriptional repressor Gfi-1 was reduced in IL-7Rα high vs. IL-7Rα low CTLs, unlike that of other transcriptional regulators tested (GABPα and Gfi-1B). Importantly, suppression of GFI expression by transfection of specific siRNAs in primary CD8+ T cells lead to a concomitant increase in IL-7Rα gene expression.

**Conclusions:** It appears that IL-7Rα low CTLs are still able to respond to cytokines important in CTL growth and differentiation other than IL-7, at the level of STAT signaling and results support a role for a transcriptional repression mechanism involving Gfi-1 in the regulation of IL-7Rα expression in these cells.

**Contact Information:** Marko Kryworuchko, Tel: 613-737-7600 x2312, Email: MKryworuchko@cheo.on.ca

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### INTRACELLULAR HIV-NEF DOWNREGULATES LPS-INDUCED IL-12P40 EXPRESSION BY INHIBITING JNK-ACTIVATED NFκB IN HUMAN MONOCYTIC CELLS

Wei Ma; Sasmita Mishra; Jyoti P. Mishra; Jonathan B. Angel; Ashok Kumar
1-Pathology and Laboratory Medicine Department, Research Institute, CHEO, University of Ottawa; 2-Biochemistry, Microbiology and Immunology Department, Research Institute, CHEO, University of Ottawa; 3- Infectious Disease & Vaccine Research Centre, Research Institute, CHEO, University of Ottawa

**Plain Language Summary:** Impaired cellular immunity because of dysregulation of Th1 cytokines is a major feature of AIDS. Interleukin-12 (IL-12) is an important Th1 cytokine, which plays a critical role in cellular immunity by producing IFN-α from T and NK cells. Biologically active IL-12 is a 70 kD lycoprotein composed of two disulfide-linked subunits, p35 and p40. The p40 subunit is an appropriate indicator for IL-12 due to its expression in IL-12p70 producing cells including monocytes/macrophages in response to various stimuli, such as bacterial endotoxin, LPS. However, how LPS induces IL-12p40 in monocytes is not clear. A severely decreased IL-12, and in particular, IL-12p40 production has been found in PBMCs and macrophages from HIV positive individuals and is believed to be correlated to HIV-associated immunodeficiency. The mechanism underlying the impaired IL-12 production in HIV infected monocytes/macrophages remains unknown. HIV-1 Nef protein, an AIDS pathogenetic factor, has been shown to downregulate Th1 cytokines. In this study, we investigated if decreased IL-12p40 production in HIV-1 infection is modulated by Nef protein in LPS-activated human monocytic cells. To address this issue, we first investigated the potential signaling pathways in the regulation of IL-12p40 in LPS-activated human monocytic cells. We then used retrovirally expressed Nef as suppressive molecule to investigate whether signaling pathways are responsible for IL-12 dysregulation in Nef-infected human monocytic cells.

**Objective:** To study the involvement of intracellular signaling pathways in the process of HIV-Nef mediated downregulation of IL-12.

**Methods:** We used retroviral expressed HIV-Nef to infect THP-1 cells and monocytes. Throughout our experiments, we used various pharmacological inhibitors and dominant negative constructs to determine the involvement of signaling molecules. We also performed Western Immunoblotting and RT-PCR to quantitate the expression of protein and mRNA. Luciferase assay and Electrophoretic mobility shift assay were conducted to study the involvement of transcription factors.

**Results:** We first demonstrated that LPS-induced IL-12p40 production in human monocytic cells is regulated by NFκB and AP-1 transcription factors through the activation of two distinct upstream signalling pathways namely the c-Jun amino-terminal kinase (JNK) and the calmodulin-dependent protein kinase-II (CaMK-II)-activated PI3K pathway. Furthermore, we show that intracellular nef expressed through transduction of monocytes with retroviral-mediated Nef gene inhibited LPS-induced IL-12-p40 expression. HIV-Nef also inhibited IL-12p40 transcription by selectively inhibiting LPS-activated JNK without affecting the activation of p38 and Erk MAPK and the calcium signalling including calcium influx and CaMK-II. In addition, HIV-nef inhibited JNK-activated NFκB without affecting the AP-1 activity. Taken together, our results suggest for the first time that intracellular HIV-Nef

down regulates LPS-induced IL-12p40 expression in human monocytic cells by selective inhibition of the JNK-activated NFκB without affecting the CaMK-II-activated PI3K pathway. These results further suggest that the inhibitory effect of HIV-Nef on JNK activation may have broad implications with respect to the inhibition of Th1 responses.

**Conclusions:** Our results suggest that intracellular Nef downregulates IL-12p40 in human monocytes through its inhibitory effect on JNK and NFκB. These studies may provide new therapeutic tools for the treatment of inflammation and autoimmune diseases and a further understanding for significant functions of intracellular Nef in AIDS pathogenesis.

**Contact Information:** Sasmita Mishra, Tel: 613-737-7600 x3919, Email: sasmishra@hotmail.com

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### 'FREAKING,' 'JONESING' AND 'COMING DOWN': AN ANALYSIS OF QUALITATIVE COMMENTARY BY DRUG USERS REGARDING THE POTENTIAL ESTABLISHMENT OF A SUPERVISED CONSUMPTION SITE IN TORONTO

Christopher Smith [2]; Peggy Millson [1]
1-HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto; 2-Graduate Programme in Communication and Culture, York University

**Plain Language Summary:** Supervised consumption sites (SCSs) are believed to reduce the rate of HIV transmission among street-level injection drug users. This paper investigates drug users' perceptions regarding the potential establishment of a (SCS) in downtown Toronto. Findings reveal a level of suspicion and wariness among drug users regarding SCS facilities, indicating the need to better understand how drug users perceive and experience harm reduction services and initiatives. Further analysis of both drop-in centres and transitional housing initiatives designed for people who use drugs can help identify the challenges, tensions and conflicts underlying the potential establishment of a SCS in Toronto.

**Objective:** Supervised consumption sites remain the most contested aspect of harm reduction policy in Canada. While significant research points to the role of SCSs in reducing both HIV and HCV seroconversion, and crime associated with illicit drug use, there is little research in the Canadian context concerning how drug users themselves perceive such facilities.

**Methods:** Qualitative commentary drawn from interviews with drug users in Toronto during the second phase of the federal I-TRACK survey was collected and analyzed. While the vast majority of addiction research is characterized by quantitative approaches, this paper examines drug user perceptions of SCS facilities through the voices and language of drug users themselves.

**Results:** Findings reveal that drug users in Toronto express a high level of wariness and suspicion regarding the notion of establishing a SCS. Several clear themes emerged in the analysis, including the tension between security concerns and surveillance paranoia, the differing needs and perceptions of housed versus homeless drug users, the difference between 'clean' and 'using' spaces, the recognition of distinct social / geographical drug using communities, and questions relating to the specificity of crack culture, encapsulated by street terminology such as 'freaking', 'jonesing', and 'coming down'.

**Conclusions:** Examining drug users' perceptions of harm reduction initiatives such as SCSs can help addiction researchers better understand the challenges, tensions and conflicts underlying the potential establishment of a SCS in Toronto. Demonstrating the need for more engaged, qualitatively driven research into the various social and geographical communities of drug users in Toronto, the analysis of drug users' commentary provides a number of clear starting points for further investigation. Because housing is a key underlying structural factor in contemporary debates concerning harm reduction, additional qualitative research regarding drop-in and transitional housing initiatives specifically designed for drug users can help in the planning, design and implementation of SCS facilities.

**Contact Information:** Christopher Smith, Tel: 416-922-0275, Email: c_smith@yorku.ca

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### THE ONTARIO HARM REDUCTION DISTRIBUTION PROGRAM: ONLY A FIRST STEP IN ENSURING EQUAL ACCESS TO HARM REDUCTION SUPPLIES IN ONTARIO

Lynne Leonard [1]; Andree Germain [1]; Emily De Rubeis [1]
1-HIV Prevention Research Team, University of Ottawa

**Plain Language Summary:** IDUs in Ontario are at high risk of contracting HCV, HIV and other infections through the sharing and use of non-sterile drug injection supplies. As such, the Ontario Harm Reduction Distribution Program (OHRDP), with funding from the Hep C Secretariat has been distributing sterile injection supplies to NEP sites in Ontario since September 2006. Through an on-going evaluation of the OHRDP we found there were significant political and ideological barriers to the distribution of these supplies that exist independently of funding concerns and must be addressed before universal access can be provided. This presentation will detail the regional differences in NEP services and the access barriers to harm reduction supplies for Ontario IDUs.

**The Challenge:** Despite the acceptance of harm reduction at the provincial level, not all regional PHUs have fully implemented NEPs. Over one-third of PHUs are not distributing all of the OHRDP supplies and others don't provide this service at all. The Ontario Public Health Branch has acknowledged the importance of comprehensive NEP services in all regions, and it is crucial that regional Boards of Health not be permitted to block these life saving initiatives because of their own ideological or political beliefs.

**Our Approach:** Phase 1 of the OHRDP Process Evaluation was administered in May 2007, eight months following the implementation of the OHRDP. Management and staff of NEPs ordering supplies from the OHRDP were asked to participate in an on-line survey related to their experiences with the program. Follow-up phone conversations were held with several sites in order to gather more detail and clarification with respect to the responses provided.

**Key Findings:** Through our research it was determined that of 36 PHUs in Ontario, only 33 had operational NEPs. In addition the NEPs of two PHUs were so small and understaffed as to render them ineffective. Of the 30 PHUs who were ordering supplies directly from the OHRDP, 35% of them had not yet received approval from their MOH to distribute all OHRDP supplies. Furthermore we found that almost half of those sites did not have information on their websites about how to access NEP services if they were required.

**Impact on Policy and Practice:** These findings have show us that the barriers to the provision of harm reduction supplies in Ontario go beyond financial considerations. They show us that even within the pubic health profession there are ideological and political barriers which must be overcome before IDUs in Ontario can have equal access to the supplies they need to protect their health. These findings should be of great concern to the Ontario Public Health Branch as their efforts to prevent the spread of disease among IDU populations are being thwarted by the ideological beliefs or political concerns of their regional PHUs and Boards of Health.

**Contact Information:** Andree Germain, Tel: 613-562-5800 x8262, Email: agermai2@uottawa.ca

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### EDUCATION LEVEL IMPACTS THE RELATIONSHIPS BETWEEN COPING, STRESS, AND IMMUNE SYSTEM FUNCTIONING AMONG MEN AND WOMEN LIVING WITH HIV

Kimberly Corace [1]; Louise Balfour [1]; Jennifer Zlepnig [1]; Giorgio Tasca [1]; Lorraine Overduin [1]; Curtis Cooper [1]; Jonathan Angel [1]; Gary Garber [1]; Paul MacPherson [1]; D.William Cameron [1]
1-The Ottawa Hospital-General Campus

**Plain Language Summary:** The present study examines the relationships between stress, depression, coping, education, and immune functioning (e.g., CD4 count) among men and women living with HIV. Results indicated that persons with lower levels of education were more stressed, depressed, and used poorer coping strategies than those with higher levels of education. Furthermore, HIV+ men and women with low education levels, who used poor coping strategies, were more vulnerable to stress and depression having a negative impact on their immune system (e.g., CD4 count).

**Objective:** Psychological factors have been shown to relate to immune functioning (e.g., CD4 count) among people living with HIV. Research has also demonstrated that lower levels of education are related to higher levels of perceived stress, higher depression, and lower immune system functioning. However, very little research has examined how coping styles may mediate the relationship between stress/depression and HIV immune system functioning among individuals with varied levels of education. This study aimed to examine the ways in which education level impacts the direct and indirect effects of stress and depression on CD4 count among men and women living with HIV (N=99).

**Methods:** Adults with HIV, who were not on antiretroviral medication, were recruited during their regular HIV clinic visit at The Ottawa Hospital. Participants completed a sociodemographic questionnaire, the Perceived Stress Scale, the CES-D (measure of depression) and the Coping Inventory for Stressful Situations. CD4 counts were measured at the same clinic visit.

**Results:** Results indicated that participants with low levels of education (high school or less) were more stressed, more depressed, and used more maladaptive coping styles than those with higher levels of education (completed college/university). In addition, perceived stress, depression and maladaptive emotion-focused coping were significantly negatively correlated with CD4 count only amongst the HIV+ persons with the lowest levels of education. Regression analyses were conducted (see Baron and Kenny, 1986) to determine whether the direct relationship between stress/depression and CD4 count was mediated by coping variables. Analyses revealed that maladaptive coping significantly mediated the relationships between stress/depression and CD4 count in HIV+ men and women with the low levels of education (high school or less).

**Conclusions:** Results suggest that lower educated men and women living with HIV who use higher levels of maladaptive coping styles are more susceptible to stress and depression negatively impacting CD4 count. Theoretical and clinical implications will be discussed.

**Contact Information:** Kimberly Corace, Tel: 613-737-8866, Email: kcorace@ottawahospital.on.ca

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### STAYING 'IN CONTROL': DRUG USE AND RISK REDUCTION STRATEGIES AMONG HIV-POSITIVE GAY MEN FROM RACIALIZED COMMUNITIES IN TORONTO

Nicole Greenspan [1]; Winston Husbands [1]; Jeffrey Aguinaldo [2]; Chris Lau [3]; James Murray [3]; Noulmook Sutdhibhasilp [4]; Rajendra Maharaj [5]; Jose Cedano [6]; Peter Ho [4]; Trevor Gray [7]
1-AIDS Committee of Toronto; 2-HIV Studies Unit, University of Toronto; 3-AIDS Bureau, Ministry of Health and Long-Term Care; 4-Asian Community AIDS Services; 5-Formerly of Alliance for South Asian AIDS Prevention; 6-Centre for Spanish Speaking Peoples; 7-Formerly of Black Coalition for AIDS Prevention

**Plain Language Summary:** Results from the 2003 Party Drugs study among gay men in the dance club scene suggest the need for health promotion approaches related to drug use among men from traditionally marginalized ethno-cultural groups. We analyzed a subset of 16 HIV-positive ethno-culturally diverse gay men to assess strategies that these men employed to reduce the possible harms associated with using drugs. Participants described safe drug use as being 'in control', being informed users, and doing drugs in socially-appropriate situations.

**The Challenge:** Harm reduction strategies currently employed by HIV-positive ethno-racially diverse gay men are not well understood, and could have important implications for secondary HIV prevention and health promotion for people living with HIV (PHAs). Previous research has shown that increased vulnerability and social exclusion affect racialized gay men who experience marginalization from their ethno-racial communities due to their sexual orientation, and from the gay community due to their ethno-racial background.

**Our Approach:** From the 74 gay men interviewed for the Party Drugs study in 2003, we analyzed the narratives of HIV-positive South Asian, East and Southeast Asian, Caribbean, Latino and Aboriginal gay men (n = 16). Respondents had (1) gone to a gay dance club in Toronto in the last three months; (2) used party drugs (i.e. Ecstasy, Ketamine, GHB, crystal meth, etc.) in the last three months; (3) identified with an ethno-racial background other than White/European; and (4) were HIV positive. A thematic analysis was conducted to summarize key drug use strategies employed by participants. We organized our findings in this straightforward manner, and specifically in relation to previous research, to allow for immediate identification of harm reduction initiatives and positive living campaigns.

**Key Findings:** Participants described a variety of strategies to reduce their risk of harm from using party drugs. Key strategies included: moderating the amount of drugs used; selecting (or avoiding) specific drugs; and spreading out use of drugs over time. Reports of these strategies revealed participants' concerns to avoid harm and addiction, and to use drugs safely, constructed as being 'in control', knowledge-informed, and context-specific in socially sanctioned situations.

**Impact on Policy and Practice:** These findings show that PHAs who use party drugs may be resistant to abstinence-based education and outreach approaches. Health promotion should frame PHAs who use party drugs as conscious, decision-making individuals. Recommended harm reduction approaches should focus on safe use and addiction avoidance, including but not limited to abstinence.

**Contact Information:** Nicole Greenspan, Tel: 416-340-8484 x250, Email: ngreenspan@actoronto.org

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### INTRODUCING MENTAL HEALTH THERAPIES IN AIDS SERVICE ORGANIZATIONS: A CBR STUDY OF KNOWLEDGE EXCHANGE

Bill Gayner [1]; Mary Jane Esplen [2,3]; Peter DeRoche [1]; Scott Bishop [4]; Lynn Kavanagh [1]; Kate Butler [2]; and the PHA ACCESS Team
1-Mount Sinai Hospital; 2- University Health Network; 3-University of Toronto; 4-Private Practice

**Plain Language Summary:** PHA ACCESS is a community-based research (CBR) capacity building project designed to help increase access for people living with HIV to mental health services by training and supporting staff and volunteers in community-based AIDS organizations (CBAOs) to provide new, evidence-based interventions. Our research seeks to assess and reflect on the effectiveness of the interventions, training procedures, and process of collaboration.

**The Challenge:** Living with HIV can cause distress, anxiety and depression. Access to mental health services is limited and many people are averse to seeking services in hospitals and mental health organizations because of stigmatization and fear of being identified as HIV+. The challenge, therefore, is to adapt therapy modalities currently used in hospital settings in order to respond to these issues and provide more accessible services.

**Our Approach:** PHA ACCESS is a community-hospital collaboration involving a Toronto-based hospital HIV clinic and seven CBAOs. CBAO staff were trained to offer three evidence-based modalities (Mindfulness, Narrative (Writing) and Art). CBR and knowledge exchange were used to support learning, program refinement, and future program development in Ontario. In our examination of client impact, measures were administered to clients before, during and after the interventions; and they participated in in-depth interviews. CBAO staff who received training and were supported to provide counseling participated in in-depth interviews or focus groups to assess the training effectiveness and to provide recommendations for intervention adaptation and training. PHA ACCESS co-investigators participated in focus groups to reflect on the collaborative process and model. Document review was used to examine the minutes of team meetings and other written materials in support of our study of the collaborative process. Qualitative outcome data were analyzed through repeated measures tests and ANOVAs. Qualitative data were analyzed using qualitative thematic analysis.

**Key Findings:** We will present demographic, baseline, and preliminary quantitative outcome data and preliminary qualitative data.

**Impact on Policy and Practice:** Safe and effective delivery of these mental health services is enabled through a rigorous review and refinement. This project builds community capacity with respect to service delivery, community-based research, through helping to address social determinants of health for PHAs by: (1) increasing access to mental health care, (2) ameliorating stigmatization, marginalization, and cultural issues, (3) empowering community advocacy for PHAs in the mental health system, (4) strengthening PHA community-building (5) improving PHA mental health and quality of life, and (6) strengthening relationships among collaborating organizations.

**Contact Information:** Bill Gayner, Tel: 416-586-4800 x8647, Email: bgayner@mtsinai.on.ca

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### MINDFULNESS FOR MEN LIVING WITH HIV

Bill Gayner [1]; Mary Jane Esplen [2,3]; Peter DeRoche [1]; Scott Bishop [4]; Lynn Kavanagh [1]; Kate Butler [2]
1-Mount Sinai Hospital; 2- University Health Network; 3-University of Toronto; 4-Private Practice

**Plain Language Summary:** In this randomized controlled study, we compared Mindfulness-Based Stress Reduction (MBSR) groups with “treatment as usual” in our psychiatry clinic and referral network for men living with HIV. While mindfulness group participants did the same as the comparison group in terms of reductions in anxiety, depression, worry and rumination, they did significantly better in terms of developing mindfulness skills (for example, being curious about difficult thoughts and emotions while knowing that “thoughts aren’t facts”) as well as developing increased interest and enthusiasm in their lives. Six months after the mindfulness group, mindfulness group participants also showed significant decreases in responses to HIV-related worries, especially in terms of decreases in their attempts at avoiding these worries, a coping style closely associated with psychological suffering. We concluded MBSR has a significant role to play in the treatment of gay men within the array of services provided by a psychiatric clinic and its referral network.

**Objective:** The primary objectives of this randomized controlled trial were to assess Mindfulness-Based Stress Reduction (MBSR) in reducing stress and psychological distress (i.e. anxiety, depression, HIV-related distress) and pain and improving overall psychological well-being and quality of life for men living with HIV. A secondary aim was to test if decreases in anxiety and depression were mediated by decreases in worry and rumination respectively.

**Methods:** A total of 117 participants were randomized 2:1 to MBSR or treatment as usual (TAU). TAU required no new psychosocial or psychopharmacological interventions within 2 months of the start of the MBSR group or during the 8-week intervention. A standardized battery of questionnaires was administered pre and post intervention. Questionnaires were mailed at 6-month follow-up to assess the maintenance of therapeutic effects and ongoing use of the intervention.

**Results:** Post intervention, both arms showed significant decreases in almost all measures. MBSR participants (including MBSR drop-outs) showed significant improvements compared to TAU in mindfulness skills (Toronto Mindfulness Scale) and positive affect (PANAS); MBSR graduates also had less negative affect (PANAS). At 6 months, MBSR participants showed significantly better outcomes in mindfulness skills, positive and negative affect, and stress-response symptoms (Impact of Event Scale).

**Conclusions:** The study indicates that mindfulness-based interventions are promising for this population. Within the context of the array services provided by a psychiatric clinic and its referral network, MBSR has a significant role to play in the treatment of gay men living with HIV and struggling with chronic psychological issues.

**Contact Information:** Bill Gayner, Tel: 416-586-4800 x8647, Email: bgayner@mtsinai.on.ca

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### FACTORS ASSOCIATED WITH GIVING AWAY USED INJECTION EQUIPMENT

Carol Strike [1,3]; Cass Wender [2]; Daniel Buchman [3]; Susan Anstice [1,3]; Brian Lester [2]; Nick Scrivo [2]; Janine Luce [1]; Russell Callaghan [1]; Margaret Millson [3]; Community Investigators [2]
1-Centre for Addiction and Mental Health; 2-AIDS Committee of London; 3-University of Toronto

**Plain Language Summary:** Efforts to reduce HIV transmission among injection drug users (IDUs) focus on reducing sharing of needles and other injection related equipment. While reports of recipient sharing (re-using a needle or equipment) have been on the decline, the reports of giving away used equipment have not. In this investigation, we focus on factors associated with distributive sharing (giving away used equipment).

**The Challenge:** To reduce distributive sharing of injection equipment, it is important to better understand factors associated with this form of HIV risk behaviour.

**Our Approach:** We interviewed 145 current injectors in London, ON and asked them about their injection practices, risk behaviours, service use, HIV and HCV status and physical and mental health status. We analyzed the data to determine what factors are associated with giving away used injection equipment.

**Key Findings:** Factors independently associated with distributive sharing varied by the type of equipment. IDUs with a history of cocaine/crack injection had the highest odds of distributing cookers (OR=5.67), followed by individuals with an Addiction Severity Index (ASI) composite score indicative of a mental health problem (i.e., ≥0.4; OR=3.257). IDUs aged 30 and over (OR=0.344) were considerably less likely than younger IDUs to distribute cookers. The odds of distributing injection water were high for IDUs who had a history of injecting methadone (OR=3.116) and injecting other stimulants (OR=2.555). Men were much more likely than women (OR=2.835) to distribute water and as were IDUs who had moved 3 or more times in the previous 6 months (OR=2.693) compared with those who had moved less. Only two factors were found to be independently associated with distributing filters: injection of cocaine/crack (OR=3.224) and having spent at least one night on the street or other public place (OR=2.479). The odds of distributing alcohol swabs were considerably decreased for IDUs who self-reported being HCV positive (OR=0.086) but high for those with ASI composite score ≥0.4 (OR=5.648).

**Impact on Policy and Practice:** These findings suggest that IDUs with the most severe addictions and who live with mental health problems and who often live in very impoverished circumstances may need extra supports to ensure sufficient injection equipment coverage. Our findings also suggest the need to coordinate needle exchange efforts with other service providers to reach IDUs who experience housing instability and mental health problems as they are more likely to engage in risk behaviours.

**Contact Information:** Carol Strike, Tel: 416-535-8501 x6446, Email: carol_strike@camh.net

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### EXISTENTIAL WELL-BEING PREDICTS THE QUALITY OF LIFE OF PERSONS LIVING WITH HIV

Fotini Zachariades [1,2]; Kim Corace [1]; Louise Balfour [1]; Jean-Pierre Routy [3]; Cecile Tremblay [4]; Jonathan Angel [1]
1-The Ottawa Hospital, General Campus; 2-Fielding University, Santa Barbara, California, USA; 3-Montreal Chest Hospital; 4-CHUM Montreal

**Plain Language Summary:** Research studies show that support exists for the role of existential well-being (EWB) in improving the physical and mental health of persons suffering from a variety of illnesses in general, and HIV/AIDS in particular. However more research is needed in order to understand how spiritual existential factors may help in improving coping with and living with HIV/AIDS.

**The Challenge:** Little research exists in specifically examining the relationship between Existential Well-Being and the quality of life (QOL) of persons living with HIV. More studies are needed to understand how spiritual and existential factors may promote coping strategies, well-being, and quality of life among people living with HIV/AIDS.

**Our Approach:** The current study examines health-related Quality Of Life of persons with HIV and investigates the relationship between Existential Well-Being and health-related Quality Of Life. The sample (N=49) consists of HIV-positive adults recruited across three Canadian sites as part of a larger multi-centered therapeutic vaccine trial. Participants completed measures of health-related Quality Of Life (Short Form-36 Health Survey) and Existential Well-Being (Existential Well-Being Scale). Statistical analyses were conducted. Specifically, student t tests were used to compare the mean Quality Of Life subscale scores of participants in this trial with age-matched Canadian norms.

**Key Findings:** Results show that the scores of the HIV-positive participants did not statistically differ from the Canadian norms (of non-HIV positive individuals) except on one subscale, Mental Health, where the HIV-positive participants scored significantly lower ($t = 2.543$, $df = 546$, $p = .01$) than the Canadian normative data. Correlational analyses indicated that Existential Well-Being was significantly positively correlated with physical Quality Of Life (e.g., General Health: $r = .51$, $p < .01$) and mental Quality Of Life (e.g., Mental Health: $r = .59$, $p < .01$).

**Impact on Policy and Practice:** Clinical implications will be discussed in terms of psychosocial support and interventions. In particular, the role of incorporating spiritual and existential factors within psychosocial interventions will be addressed, as well as how such factors can improve coping strategies and well-being both in the short-term and in terms of influencing longer-term adjustment to illness (HIV/AIDS), and physical and mental health outcomes.

**Contact Information:** Fotini Zachariades, Tel: 613-722-9005, Email: fzachari@hotmail.com

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**STICKING POINTS: BARRIERS TO ACCESS TO NEEDLE AND SYRINGE PROGRAMS IN CANADA**

Alana Klein [1,2]; Richard Elliott [1]; Joanne Csete [1]; Richard Pearshouse [1]
1-Canadian HIV/AIDS Legal Network; 2-Faculty of Law, McGill University

**Plain Language Summary:** Needle and syringe programs (NSPs) are a proven, cost-effective way of reducing HIV transmission among people who use drugs (PUDs). However, barriers persist that prevent PUDs from free access to sufficient sterile injection equipment. We gathered data from across Canada, identified key barriers and present recommendations to address those barriers.

**The Challenge:** It is estimated that NSPs currently distribute only about 5% of the syringes needed to ensure sterile equipment at every injection. It is difficult to assess NSP coverage in Canada because of variability in distribution modes, the definition of "site" or "program", and tracking of programs and coverage.

**Our Approach:** We conducted a literature review and interviews with key informants – including government officials, NSP staff and PUDs – in every jurisdiction. We analysed the available evidence in light of governments' human rights obligations to take positive measures to prevent and control diseases. A first draft of the research report was circulated among stakeholders before being finalized. To the best of our knowledge, this 2007 report represents the first comprehensive assessment of NSP access, and the barriers thereto, across Canada.

**Key Findings:** We identified the following barriers to NSP access: (1) criminal laws on drugs and drug paraphernalia; (2) law enforcement practices; (3) judicially-imposed conditions restricting access to NSPs; (4) stigma and privacy concerns; (5) community resistance; (6) inappropriate use of municipal by-laws; (7) insufficient funding; and (8) barriers related to program design (e.g., restricted operating hours, inadequate geographic coverage, restrictions on amount of injection equipment distributed per visit; reluctance of some NSPs to distribute safer drug use materials other than needles and syringes; not meeting users' preferences for mode of service delivery, etc.).

**Impact on Policy and Practice:** Recommended actions include: (1) Provincial/territorial governments should require needs assessments in every health region and, where needed, explicitly require NSPs as required health services, supported by adequate funding. (2) Federal government funding for HIV, HCV and Canada's national drug strategy should include support for harm reduction services, including NSPs. (3) Federal criminal laws on drugs and drug paraphernalia should be amended to remove the shadow of criminality over NSPs. (4) Judges should not impose restrictions preventing access to harm reduction services. (5) Programs should be (re)-designed, in consultation with PUDs, with the primary goal of maximizing access to sterile injection equipment. (6) Municipalities should ensure zoning by-laws do not create hurdles, such as community approval requirements, for establishing NSPs.

**Contact Information:** Richard Elliott, Tel: 416-595-1666, Email: relliott@aidslaw.ca

## Vulnerable Populations

### 236

**WHAT DO TEENS REALLY WANT TO KNOW? SEXUAL HEALTH QUESTIONS ASKED IN TORONTO TEEN SURVEY WORKSHOPS**

Crystal Layne [1]; Ana Bobesiu [1]; Susan Flynn [1]; Sarah Flicker [2]; June Larkin [3]; Robb Travers [4]; Jason Pole [5]; Peggy Harowitz [2]; Emily Dauria [4]; Hazelle Palmer [1]
1-Planned Parenthood Toronto; 2-Faculty of Environmental Studies, York University; 3-Women and Gender Studies Institute, University of Toronto; 4-Ontario HIV Treatment Network; 5-Department of Public Health Studies, University of Toronto

**Plain Language Summary:** The aim of the Toronto Teen Survey (TTS) is to gather information from youth on assets, gaps and barriers that currently exist in sexual health education and services and to use the information to develop a city-wide strategy to increase positive sexual health outcomes for diverse Toronto youth. The project uses the community-based participatory research model to engage youth and service providers over the course of the project. Over 1,200 teens participated in the project by attending one of ninety TTS workshops held primarily in community service agencies.

**Objective:** Although there are various methods for teens to access sexual health information (e.g. internet, health care providers) very little is known about what information they would like to receive. Youth may be hesitant to vocally ask questions about what they really want to know out of a fear of them being identified and negatively judged by their peers.

**Methods:** Phase two of this project involved having members of our Youth Advisory Committee (YAC) facilitate sexual health workshops with teens as our main method of data collection. Using the peer-to-peer model, YAC members administer the survey and facilitate a question and answer session where participants submit anonymous written questions to be answered by the facilitators. The participants' questions were coded based on topic and analyzed to identify common themes and areas for further exploration.

**Results:** A total of 1,014 questions were submitted within the 90 workshops. The questions were coded by the type of topic it addressed. Example topics include: contraception methods, sexual orientation, sexually transmitted infections, relationships, and pregnancy. A preliminary analysis of the data show a high proportion of the questions attempt to address myths that may be prevalent in youth subculture. Common topics included questions related to sex acts and behaviors, sexual readiness, and pregnancy.

**Conclusions:** In order to improve STI/HIV prevention programs and the efficacy of sexual health education for Toronto's diverse communities, it is important to identify what topics teens want their education to address as this has been shown to increase retention and the likelihood of using safer sex practices. This study has demonstrated that youth do have questions about sexual health issues that are relevant to them and are willing to request this information when given a format that allows for them to be candid while preserving their privacy and confidentiality.

**Contact Information:** Crystal Layne, Tel: 416-961-0113 x253, Email: clayne@ppt.on.ca

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**"IT'S A TECHNICAL PROBLEM": YOUNG LESBIAN AND BISEXUAL WOMEN'S PERCEPTIONS OF HIV RISK AND USE OF PREVENTION STRATEGIES**

Jaime McCauley [1]; Barry Adam [1]; Sandra Bortolin [1]; Catherine Brooke [1]
1-University of Windsor, Department of Sociology and Anthropology

**Plain Language Summary:** The objectives of this study are: 1) assessing how self-identified lesbian and bisexual young women perceive potential risk of HIV infection and how they minimize that risk, 2) identifying where these young women get information about HIV prevention and whether the information is helpful. Our project consists of 10 interviews with lesbian and bisexual women ages 16-22 concerning their perception of HIV risk and use of safer sex practices. Results suggest many respondents believe lesbians and bisexual women have no or low risk of HIV infection through sex with women and do not utilize safer sex practices because of this belief. Findings indicate the majority of participants receive information on HIV/AIDS through media sources (television and internet) and conversations with their LGBT peers.

**The Challenge:** Our aim is to assess how young lesbian and bisexual women conceptualize their risk for HIV infection, what information is influencing their conceptualization of this risk, whether they are aware of effective prevention strategies, and why they do or do not use prevention strategies.

**Our Approach:** Subjects were recruited from the greater Windsor area through local LGBT youth support groups, the placement of advertisements in local city, college, and university newspapers, and the use of snowball sampling procedures. Each participant answered a questionnaire that measured sexual behavior and use of protection, and in-depth interviews were conducted to assess beliefs and attitudes about risk, prevention strategies, and access to information.

**Key Findings:** Key findings indicate that most of these young women perceive low or no risk of HIV infection from sexual contact with other women. Many found prevention strategies cumbersome to sexual encounters (one stating that "it's a technical problem…"). Little information was presented to them through school or family sources, and this information was often abstinence based, targeted toward heterosexuals, and included no strategies for prevention. Additionally, when HIV/AIDS was mentioned in the classroom, it was from a chemical or biological perspective where the science of the disease was presented with no discussion of risk or prevention. Information from peers and media sources was most helpful, but sometimes incorrect and/or contradictory. Outreach and education specifically targeting lesbian and bisexual women is virtually non-existent.

**Impact on Policy and Practice:** Because little attention is paid to lesbian and bisexual women in terms of HIV education and prevention (especially among youth) this research is an important first step in the development of successful HIV education and outreach geared toward this underserved population.

**Contact Information:** Jaime McCauley, Tel: 519-962-9629, Email: mccaulej@uwindsor.ca

## 238

### UNDERSTANDING FACTORS THAT PROMOTE AND HINDER PARTICIPATION IN WOMEN LIVING WITH HIV

Seanne Wilkins [1]; Patty Solomon [1]
1-School of Rehabilitation Science, McMaster University

**Plain Language Summary:** With the shift in the natural history of HIV the role of rehabilitation in managing disability has increased. This study explored the lived experience of 22 women living with HIV and the factors that promoted and hindered their full participation in their chosen community activities. Suggestions for change in policy and practice are provided.

**The Challenge:** With the shift in the natural history of HIV to an increasingly chronic episodic illness the role of rehabilitation in management of HIV related disability has increased. The World Health Organization developed the International Classification of Functioning, Disability and Health (ICF) to assist in understanding how contextual factors such as environment and personal factors relate to leading a full life. This study examined the experiences of women living with HIV, focusing on what helped and hindered full participation in their chosen community activities.

**Our Approach:** The study used qualitative, phenomenological methods. Purposeful recruitment methods identified diverse community participants. Women participated in in-depth interviews. Use of the ICF framework ensured a variety of environmental and personal factors were examined. In-depth analyses identified the emergent codes and themes related to participation.

**Key Findings:** Twenty-two women were interviewed. Women did not rank HIV and self-care as a high priority in their lives. Decreased participation was related to poverty, enduring depression and isolation, fear of disclosure, lack of supportive networks and symptoms of their illness. Many barriers to work participation existed. Women who had learned to balance their lives, who were able to access a variety of supports and who possessed a strong self-identity and purpose in life were able to participate in meaningful activities. Childcare was a major factor in all women's lives. For those participating fully, children provided a sense of involvement which lead to a more fulfilling life. For those experiencing difficulty, children were the sole source of motivation for any participation.

**Impact on Policy and Practice:** Findings point to the need for review of policies related to disability pensions to enable women to return to meaningful work. Although the women experienced ill health related to their HIV, environmental factors took precedence over personal concerns. Without supportive networks and opportunities for childcare, women are unlikely to access community rehabilitation. Findings support the need for rehabilitation at direct service levels (e.g., pain management, return to work), consultation levels (e.g., work accommodation), environmental levels (advocacy with government re: disability pensions) and the need for advocacy to support gender specific rehabilitation services at local, national and international levels.

**Contact Information:** Seanne Wilkins, Tel: 905-525-9140 x27839, Email: swilkins@mcmaster.ca

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### PERCEPTIONS OF HIV RISK AMONG LESBIAN, GAY, BISEXUAL, TRANSGENDER, & QUESTIONING YOUTH

Catherine Brooke [1]; Barry Adam [1]; Sandra Bortolin [1]; Jaime McCauley [1]
1-University of Windsor

**Plain Language Summary:** Twenty-two lesbian, gay, bisexual, transgender and questioning youth in the Windsor, Ontario area were interviewed to assess the "take home" messages they received concerning HIV prevention from school and other sources such as, media, peer groups, friends, family, and sexual partners. As LGBTQ youth mature, and enter in sexual and romantic relationships, they become part of one of the communities most at risk for HIV transmission and so need to be well-equipped to manage HIV risk. Findings indicate that school programs often do not discuss HIV prevention and when they do, material tends to be presented from a biologically-oriented and exclusively heterosexual approach. Sources of information accessed by these youths most frequently were media, friends and sex partners. These findings illustrate that LGBTQ youth need access to HIV prevention information in addition to what they "take home" from school and point to the role that needs to be filled by the media and health agencies.

**The Challenge:** To assess the "take home" messages LGBTQ youth receive concerning HIV prevention from high school and also from other sources of information such as peer groups, media and sexual partners.

**Our Approach:** Semi-structured, in-depth interviews were conducted on perceptions of HIV risk among youth and sources of prevention information.

**Key Findings:** Findings indicate that school programs often do not discuss HIV prevention, focusing more instead on abstinence-only approaches to sexuality. When HIV information is offered, the material is delivered from a heterosexist, biologically-oriented approach. The media is the most often cited source of information, for example the internet and television shows such as The L Word and Degrassi. Youth also rely on friends and sexual partners as other sources of information. Female participants did not consider HIV prevention a priority as they perceived lesbian sex as low or without risk. For all youth, knowledge about HIV prevention did not always translate into safer-sex practices. Of the 15 youth who were sexually active, 13 indicated that they had sex without using protection (i.e., condoms, dental dams) in the last 6 months. For males, concern that sex partners would think they were either HIV positive or unfaithful were the most common reasons for not using condoms.

**Impact on Policy and Practice:** Findings indicate that the take home messages from Ontario high schools are fragmentary and raise the question of the role of the media, community organizations, and health services in filling the gaps left by the education system.

**Contact Information:** Catherine Brooke, Tel: 519-980-9049, Email: brooke1@uwindsor.ca

## 240

**PUTTING DISABILITY INTO CONTEXT: FACTORS THAT INFLUENCE THE EXPERIENCES OF DISABILITY FOR ADULTS LIVING WITH HIV/AIDS**

Kelly O'Brien [1,2]; Aileen M. Davis [2,3]; Carol Strike [4,5]; Nancy L. Young [2,6]; Ahmed M. Bayoumi [1,2]
1-Centre for Research on Inner City Health, St. Michael's Hospital; 2-Department of Health Policy, Management and Evaluation, University of Toronto; 3-University Health Network, Toronto Western Hospital; 4-Centre for Addiction and Mental Health; 5-Department of Psychiatry, University of Toronto; 6-School of Human Kinetics, Laurentian University

**Plain Language Summary:** We conducted focus groups and interviews with adults living with HIV to develop a framework that describes disability. Disability was episodic and multi-dimensional including symptoms/impairments, difficulties carrying out day-to-day activities, challenges interacting in society, and uncertainty. Environmental (social support and stigma) and personal factors (living strategies and personal attributes) had the potential to make disability worse or better. These factors should be considered by providers when measuring disability experienced by people living with HIV.

**The Challenge:** To describe factors that influence the experiences of disability from the perspective of adults living with HIV within a larger conceptual framework.

**Our Approach:** We conducted focus groups and interviews with adults living with HIV who experienced an episode of illness. We asked participants to describe their health-related challenges, the physical, social and psychological areas of their life affected, and the impact of these challenges on their health. We used grounded theory to develop a conceptual framework that described the consequences of living with HIV. Within this framework, we focused on factors that influenced how these consequences were experienced by adults living with HIV.

**Key Findings:** We recruited 38 participants (21 men, 16 women, 1 transgendered person) for one of 4 focus groups or 15 face-to-face interviews. Participants had a median time since HIV diagnosis of 9 years (interquartile range: 5-9); 25 (66%) were taking antiretrovirals and 19 (50%) had a nadir CD4 count <200 cells/mm3. Participants conceptualized disability as episodic, characterized by unpredictable periods of wellness and illness. Disability included four dimensions: symptoms/impairments, difficulties carrying out day-to-day activities, challenges to social inclusion, and uncertainty. Four main contextual factors influenced these dimensions: 1) social support; 2) stigma; 3) living strategies, such as seeking social interaction with others, maintaining sense of control over life and illness, and attitudes and beliefs; and 4) personal attributes such as aging and gender. We categorized the first two factors as extrinsic and the latter two as intrinsic.

**Impact on Policy and Practice:** Both extrinsic and intrinsic factors set the context in which adults living with HIV experience disability and provide a more comprehensive understanding of this concept. Future work should address how contextual factors can be considered by health providers and policy makers interested in measuring disability experienced by adults living with HIV.

**Contact Information:** Kelly O'Brien, Tel: 416-978-0565, Email: kelly.obrien@utoronto.ca

## 241

**VISIBLY HIDDEN: RETHINKING BMSM AND HIV PREVENTION**

David Lewis-Peart [1,2]
1-Black Coalition for AIDS Prevention; 2-African and Caribbean Council on HIV in Ontario

**Plain Language Summary:** Black gay, bisexual, and straight-identified men who have sex with men in Toronto, are at heightened risk of HIV infection due to a number of factors, which include but are not limited to, race, class, gender, and homophobia. This, compounded by an absence of targeted services, community space, and historical presence in research increase BMSM isolation and subsequent vulnerability. The range of issues speak to a need for targeted, and inclusive programming, research and services for Black MSM in Toronto.

**The Challenge:** Black men who have sex with men represent an increasing number of HIV infections in Ontario, despite this fact there are few existing BMSM specific research, services, and strategies addressing this issue. The goal of this Toronto-focused qualitative report was to determine common themes and trends for BMSM in relations to their needs, capacities, and barriers to HIV prevention support, as well as to identify BMSM-related health and social services and to assess gaps in service. From this priorities have been identified, and recommendations made with the intention of aiding the development of BMSM specific prevention and intervention strategies.

**Our Approach:** For this report, 25 Key informants were selected based on their work as researchers, and service providers within the HIV/AIDS, Youth, and African/Caribbean service sector. Participant feedback was audio recorded, discussions reviewed, and common themes identified. Information compiled from these interviews were then corroborated with local and international research and epidemiological data. Content findings were then further reviewed by a panel of local experts and a BMSM youth sub-committee to validate the identified themes and recommendations.

**Key Findings:** Black men who have sex with men represent the largest number of new HIV infections among racialized MSM in Toronto. This increased vulnerability for Black MSM and particularly BMSM youth can be directly related to the multiple identities and marginal social locations many BMSM negotiate throughout their lives. The layered effects of homophobia, racism, poverty, and HIV stigma as well as a lack of relevant and inclusive service provision, severely impacts the ability for many BMSM to access services that may assist in the reduction of risk.

**Impact on Policy and Practice:** Effective sexual health and HIV prevention programs are required that recognize the varied, dynamic and situational identities lived by Black men who have sex with men. Recognizing this, programming for Black men must focus not only on the dissemination of relevant information but on the building of practical skills for changes in social and sexual behaviour also.

**Contact Information:** David Lewis, Tel: 416-912-3794, Email: david.davidlewis@gmail.com

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### ASIAN MSM IN HIV PREVENTION LITERATURE: A CRITICAL ANALYSIS

Jeffrey P. Aguinaldo [1,2]
1-HIV Social, Behavioural, and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto; 2-Department of Sociology, Wilfrid Laurier University

**Plain Language Summary:** Epidemiological research has consistently demonstrated a low prevalence of HIV/AIDS within Asian populations in the North American context. One would think that such findings would prompt further research to investigate the unique factors that prevent the proliferation of HIV/AIDS within these populations and that enable Asian MSM to protect themselves and each other from the transmission of HIV. However, such research has not been forthcoming. Typically, researchers hold HIV/AIDS prevalence data on Asian populations with methodological suspicion and portray Asian MSM and their cultures as 'problems' that HIV prevention must 'overcome.' In this paper, I undertake a critical analysis of HIV prevention literature to explore the social construction of Asian MSM.

**Objective:** (i) To explore the ways that Asian MSM are represented in the HIV prevention literature, and (ii) to assess the political costs and benefits of representing Asian MSM in these ways.

**Methods:** The literature was collected through standard academic databases using a combination of keywords including Asian, MSM, gay, homosexual, HIV, AIDS, risky sex. The present analysis focuses on research in North America. The texts were read, not for what they can tell us about Asian MSM, but for what they can tell us about how Asian MSM are represented in the HIV prevention literature.

**Results:** Three recurring themes emerged: (i) Asian MSM are sexually ignorant and unable to negotiate safer sex practices, (ii) Asian MSM are psychologically damaged, and (iii) Asian MSM willingly place themselves at risk for HIV.

**Conclusions:** While Asian MSM are infinitely complex and diverse, HIV researchers must speak about Asian MSM only in ways that do not threaten the racist social order. To ensure HIV prevention efforts are inclusive of Asian MSM, researchers must narrate the experiences of Asian MSM in accordance to the very accounts that reinforce their oppression. Put simply, researchers must depict Asian MSM as sexual weaklings, as emotionally troubled, and as cultural dupes who willingly place themselves at risk, not because these accounts are necessarily true, but because this appears to be the only way to expose and redress the habitual exclusion of Asian MSM in HIV prevention efforts. Although conceding that we, as researchers, must invoke these accounts if only for this pragmatic purpose, I urge that we not lose sight of the broader political implications of our work and constantly remind ourselves of the social justice goals toward which we should ultimately strive.

**Contact Information:** Jeffrey Aguinaldo, Tel: 416-978-1200, Email: jeffrey.aguinaldo@utoronto.ca

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### SOURCES OF HIV-RELATED INFORMATION AND SUPPORT, AND VIEWS OF THE EPIDEMIC: A QUALITATIVE, COMMUNITY-BASED RESEARCH (CBR) STUDY WITH GAY MEN IN A SMALL CANADIAN CITY

Stevenson Fergus [1,2]; Marney McDiarmid [1,2]; Joseph Babcock [2,3]; Ryan Jamieson [1,3]; Tony Piper [2]; Jim Puckalo [2]; Kevin Sosnowski [2]; Bob Stewart [2]; 1-Queen's University; 2-HIV/AIDS Regional Services; 3-Kingston Area Men's Project Community Advisory Board

**Plain Language Summary:** We interviewed groups of men from the gay community in Kingston, Ontario, to learn about what they think about HIV, and if they talk about HIV with each other. Men said that they do not talk about HIV very often.

**The Challenge:** Much of the HIV prevention research among gay men in Canada has been conducted with men from large urban centres. Little is therefore known about how gay men in small Canadian cities obtain information or support concerning HIV, or how they conceptualize HIV within their communities. We do not know how HIV prevention interventions or messages developed for men in larger cities, such as interventions involving peers as natural helpers, may most effectively be used with this community.

**Our Approach:** We conducted a CBR project in the gay male community of Kingston, Ontario. CBR involves full participation by community members in all aspects of the research, ensuring appropriateness and relevance of methods and findings. This exploratory study included 11 focus groups with a total of 55 participants, and individual interviews with 4 key informants. Two of the focus groups were made up exclusively of HIV-positive men. Topics included being gay and out in Kingston, Kingston's gay community, homophobia, and HIV stigma and services. We used a participatory, constructivist grounded theory approach to analyze the data.

**Key Findings:** Participants rarely discussed HIV with their peers and revealed that most participants felt a discussion of HIV was only relevant to sexual encounters. This suggests that HIV is discussed only in the context of individual risk reduction, and is not discussed as a larger social phenomenon affecting the gay male community. Some participants noted this might be different from experiences of gay men in larger metropolitan areas such as Toronto, where rates of HIV are higher and the topic of HIV may therefore be more openly discussed.

**Impact on Policy and Practice:** The implementation of HIV prevention interventions, particularly those involving natural helpers, may require enhanced attention to ensure that the men involved are receptive to discussions about HIV. Men in smaller cities may also benefit from consciousness-raising interventions that stress the social characteristics of the HIV epidemic, and its influence on gay communities.

**Contact Information:** Stevenson Fergus, Tel: 613-533-6000 x7, Email: ferguss@post.queensu.ca

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### APPLICATION OF THE THEORY OF GENDER AND POWER TO IDENTIFY PREDICTORS OF CONDOM-USE RISK AMONG MIDDLE EASTERN AND/OR ARAB CANADIANS IN HETEROSEXUAL RELATIONSHIPS

Nour Schoueri [1]; Sandra Bullock [1]
1-University of Waterloo, Department of Health Studies & Gerontology

**Plain Language Summary:** The study explored associations between factors derived from the application of the Theory of Gender and Power (TGP) as they relate to HIV-risk behaviour among Middle Eastern/Arab Canadians. This area deserves increased attention, as the proportion of HIV incident cases among Canadian women—due to heterosexual transmission—is increasing.

**Objective:** To identify the predictors of condom-use risk among Middle Eastern/Arab Canadians.

**Methods:** A web-based survey was administered to self-identified Middle Eastern/Arab Canadians aged 18-35 years, who were living in Canada, heterosexual, and in a relationship of at least 21 days. Multivariate regression analyses were used to assess factors associated with condom-use risk. Analyses were stratified by gender.

**Results:** The study sample consisted of 157 participants, with a mean age of 22.7 years, more female participants (65.4%), and females were more likely to have an older partner and to be virgins than males. Less than a third (27.5%) of sexually active participants in this sample reported using condoms every time they had sex and participants reported a mean of 4.3 lifetime sexual partners. Factors associated with condom-use risk varied greatly between genders. Among females, being controlled by their partners, having negative attitudes towards condoms, and having low self efficacy towards practicing safer sex were predictive of condom-use risk. Among males, not believing they could get their partners to use condoms, rarely attending religious services, and not being worried about getting HIV were predictive of condom-use risk.

**Conclusions:** The application of the TGP to this sample was moderately successful in predicting condom-use risk among males. However, it was not as successful in predicting condom-use risk among females. Many factors associated with HIV risk have been identified in this study that could be used to create interventions designed to increase equality within Middle Eastern/Arab Canadian relationships. However, issues are discussed that still need to be addressed in future research.

**Contact Information:** Nour Schoueri, Tel: 416-318-6509, Email: nschouer@ahsmail.uwaterloo.ca

## 245

### WHO FEELS IT KNOWS: THE CHALLENGES OF HIV PREVENTION FOR YOUNG BLACK WOMEN IN TORONTO

Shani Robertson [1, 2]
1-Black Coalition for AIDS Prevention; 2-African and Caribbean Council on HIV/AIDS in Ontario

**Plain Language Summary:** Many would say Black women face the same issues as anyone else. This study points to a clear answer: “Black women are Black women”. It is not that the issues are exclusive to Black women. Rather, it is the way the issues are uniquely interconnected in Black women’s lives that create the need for a new approach to HIV prevention. This study confirmed that issues such as poverty, sexual violence and male partner health, greatly increases the chance of a young Black woman contracting HIV.

**The Challenge:** No HIV prevention strategies in Toronto have been developed to focus specifically on young Black women. Consequently, the first step in developing HIV prevention programming is to gather and assess the available evidence that may inform new HIV prevention initiatives. The goal of the study was to determine what issues young Black women are facing that prevents them from making healthy choices about their sexual relationships, and ultimately protecting themselves from HIV.

**Our Approach:** Thirty-six interviews were conducted with stakeholders, researchers and service providers who work with Black communities in Toronto. A literature & best practices review were conducted on issues linked to Black women’s increased vulnerability to HIV. The findings were analyzed and reviewed by a community stakeholder committee and a youth advisory committee, who validated and confirmed young Black women in Toronto.

**Key Findings:** A broad range of social issues were found to influence Black women’s risk of contracting HIV. Poverty and violence, specifically childhood sexual abuse and intimate partner violence, may increase Black women’s vulnerability to HIV. In addition, women’s vulnerability to HIV is strongly linked to characteristics of their male partners. High rates of STIs, notably chlamydia and gonorrhea in women ages 15-29, were found in neighborhoods with high concentrations of Black people. In turn, neighborhoods with high concentrations of Black people were also under-served in terms of healthcare services.

**Impact on Policy and Practice: 1)** Prevention responses must be representative of specific target populations and be ‘non-mainstream’; additionally, religious, linguistic, cultural and age differences must be taken into consideration; 2) Address the issue of multiple partners from a harm reduction perspective and promote condom use with all sexual partners; 3) Incorporate the issues of CSA and IPV into HIV and STI prevention messaging; 4) Develop sexual health information that reflects the culture and lifestyle of Black female youth; 5) Develop sexual health information that reflects the culture and lifestyle of Black female youth.

**Contact Information:** Shani Robertson, Tel: 416-887-1429, Email: wprevention@black-cap.com

## 246

**IDENTIFYING SYSTEMIC FACTORS THAT CREATE HIV VULNERABILITY FOR URBAN AND ON-RESERVE ABORIGINAL YOUTH: IMPLICATIONS FOR PREVENTION PROGRAMMING**

Christine Smillie [1]; Sarah Flicker [2]; June Larkin [1]; Jean-Paul Restoule [3]; Ruth Koleszar-Green [4]; Kevin Barlow [5]; Michelle Dagnino [7]; Claudia Mitchell [6]; Christine Ricci [2]
1-The Gendering Adolescent AIDS Prevention (GAAP) Project, University of Toronto; 2-Faculty of Environmental Studies, York University; 3-The Ontario Institute for Studies in Education, University of Toronto; 4-Social Work, Ryerson University; 5-Canadian Aboriginal AIDS Network; 6-McGill University; 7-Cavalluzzo Hayes Shilton McIntyre Cornish LLP

**Plain Language Summary:** Aboriginal youth are both over-represented in the HIV epidemic and infected at a younger age than non-Aboriginal peoples. In this paper we discuss some of the systemic factors that increase HIV vulnerability for Aboriginal youth and the relevance of these findings for prevention strategies. Through an analysis of data collected through focus groups with urban and on-reserve Aboriginal youth we report on key themes that emerged from the data: colonialism, attitudes toward Elders, condoms, and stigma. We discuss how the youth took up each theme in the context of HIV risk or prevention and the discrepancies in viewpoints within and across the focus groups. We argue that historical and contemporary issues faced by Aboriginal communities should be incorporated into both Aboriginal and non-aboriginal HIV prevention programming to help reduce the stigma that increases HIV vulnerability for Aboriginal youth.

**Objective:** Our objectives were: 1) To examine the systemic factors associated with HIV risk; 2) To compare issues of HIV vulnerability facing Aboriginal youth in different geographical locations; 3) To identify educational and community support initiatives that work for Aboriginal youth; 4) To consider the relevance of our findings for HIV prevention programming for both Aboriginal and non-Aboriginal youth.

**Methods:** We conducted focus groups with Aboriginal youth in urban and reserve settings in Ontario and Quebec. Focus groups were conducted by local youth facilitators trained by Aboriginal members of our research team.

**Results:** The youth had varied opinions on the role of colonialism in the high HIV infection rates in their community which ranged from a dismissal of the impact of colonialism to concerns that the psychological affects of colonial practices increase risk behavior. Many youth felt that Aboriginal people were viewed negatively by mainstream society and the government, a situation that increases the stigma associated with HIV in their communities. The use of condoms was limited by the resistant attitudes of young men and issues that varied between urban and on-reserve settings. The youth expressed a desire for the Elders to take a stronger role in HIV prevention education.

**Conclusions:** HIV prevention strategies should engage explicitly with connections to colonialism, racism and other systemic inequities as a way of identifying the reasons behind high risk behavior in Aboriginal youth. Elders should take a more prominent role in HIV/AIDS awareness and prevention work in their community.

**Contact Information:** June Larkin, Tel: 416-978-8282, Email: june.larkin@utoronto.ca

## 247

**DEPRESSION, FOSTERING, & ADOPTION EXPERIENCES AMONG ABORIGINAL PEOPLE LIVING WITH HIV**

Roy Cain [1]; Randy Jackson [2]; Tracey Prentice [2]; Evan Collins [3]; Judy Mill [4]; Kevin Barlow [2]
1-School of Social Work, McMaster University; 2-Canadian Aboriginal AIDS Network; 3-Dept. of Psychiatry, University of Toronto; 4-Faculty of Nursing, University of Alberta

**Plain Language Summary:** This study aims to understand how the social and cultural background of Aboriginal people living with HIV/AIDS (APHAs) shapes how they understand, experience, and respond to depression. A history of being adopted or being raised in foster care emerged as a significant issue in our interviews with APHAs. In this presentation, we will discuss how our participants viewed the link between their fostering/adoption experiences and their struggles with depression.

**Objective:** Our study examines how the social and cultural background of Aboriginal people living with HIV/AIDS (APHAs) shapes how they understand, experience, and respond to depression. In this presentation, we will discuss how our participants viewed the link between their fostering/adoption experiences and their struggles with depression.

**Methods:** In this community-based research project, we conducted 72 in-depth interviews with APHAs (men=45; women=23; and transgender=4) at various ages and stages of HIV infection in seven settings: Vancouver, Edmonton, Winnipeg, Toronto, Ottawa, Montreal and the Atlantic region. Fifteen service organizations assisted with the recruitment of participants. Interviews lasted 60 to 90 minutes. Verbatim transcripts were coded and analyzed for emergent themes.

**Results:** Twenty-three of our participants – about one-third of our sample – were raised for at least part of their childhood in foster care or in adoptive homes. The experience of being raised by people other than their biological parents, most often by non-Aboriginal parents, emerged as significant in how these participants understood their depression. They viewed their foster/adoption experience as a reason they now feel disconnected from their community and unfamiliar with its language, traditions and beliefs. Many of these participants also talked about the lack of support and abuse they experienced in their foster and adoptive homes, and how being raised in such homes made them vulnerable to racism. This background contributed to their sense of instability and helped them form an identity as an outsider. Factors such as these were seen by participants to underlie or significantly contribute to their depression.

**Conclusions:** The study illustrates some of the complexities underlying depression in the lives of Aboriginal people with HIV. Depression, which often precedes HIV, is often seen to be tied to broader issues, such as the disproportionate number of Aboriginal youths taken into care. Our interviews suggest how addressing depression among APHAs may require workers to look beyond HIV, and to consider other personal and community concerns.

**Contact Information:** Roy Cain, Tel: 905-525-9140, x27960, Email: cainr@mcmaster.ca

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### LISTENING TO THE VOICES OF WOMEN LIVING WITH HIV/AIDS: A QUALITATIVE STUDY OF PSYCHOSOCIAL IMPACT AND QUALITY OF LIFE ISSUES

Edna Aryee [1]; Terry Mitchell [1,2]
1-University of Toronto; 2-Wilfrid Laurier University

**Plain Language Summary:** In the mid-1990s, medical advances dramatically altered the experiences of living with HIV/AIDS. These advances raised new psychosocial questions such as coping strategies. In this qualitative study, I examined how 5 women living with HIV/AIDS in Ontario dealt with their daily psychosocial needs and challenges. Based on a life history methodology, responses of participants were coded and analyzed in relation to the ecological framework of psychology. The thematic analysis indicated that despite the existing medical, governmental and community support, women living with HIV/AIDS nevertheless faced numerous daily psychosocial challenges. Findings have conceptual and methodological implications for future psychosocial research on women living with HIV/AIDS.

**Objective:** Explore the psychosocial impact of living with HIV/AIDS. Explore the quality of life and coping strategies on multiple dimensions (individual, family, community, health sector and society). Explore proactive strategies for improving quality of life for women living with HIVAIDS.

**Methods:** I used a qualitative methodology, which involved life history, and community based participatory approaches. Purposive and snowball sampling procedures were used to identify the participants who were between age 16-65. Questionnaire and journal notes were the main sources of data. The questionnaire was divided in three parts; the first part had nine open-ended questions, capturing the experiences before HIV, the second parts had thirteen questions looking at the needs, challenges and psychosocial support for women living with HIV/AIDS and third part had nine questions looking at their coping strategies and strengths. The interviews ranged from two hours to three and half hours in length. The journal notes were also divided into three categories: physical, psychological and behavioural. I analyzed the data by dividing the transcripts into narratives, and then condensing them into themes. Later I transported the document into the NVIVO software programme and then picked out all the relevant.

**Results:** Data revealed the daily coping strategies of these women as well as the availability of resources and services for women with HIV/AIDS within Ontario. The participants demonstrated remarkable strengths in confronting these challenges: many managed to balance internalized stigma, exclusion, and unemployment with their survival. These women strived to progress through these challenges by developing inner strength, individual coping mechanisms and survival strategies such as prayer and forming support groups. Psychosocial challenges that were identified included: stigma and social exclusion fear of death, suicidal ideation, as well as lack of adequate or appropriate support from healthcare professionals and psychologists. In addition participants also noted frequent experiences of loneliness, housing problems, poverty and unemployment as part of their every day challenges. An important outcome of my findings is the transferability of the strengths and coping strategies of these women as a model for other women with HIV/AIDS in Africa and the world at large.

**Conclusions:** Among the participants in my research were secretaries, lab technicians and childcare workers and these women brought in their knowledge and rich experience. The call to empower women has never been more urgent. We must all act now to strengthen the capacity, resilience and leadership of women living with HIV/AIDS.

**Contact Information:** Edna Aryee, Tel: 647-345-7798, Email: korkor76p@yahoo.ca

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### SOCIAL VULNERABILITIES CONTRIBUTING TO SEXUAL RISK BEHAVIORS AMONGST ETHNO-RACIAL MSM: PRELIMINARY FINDINGS FROM A COMMUNITY BASED RESEARCH STUDY

Alan Li [1,2,4]; Devan Nambiar [3]; Maurice Poon [4,7]; Tarik Bereket [5]; Trevor Hart [6]; James Murray [8]
1-Committee for Accessible AIDS Treatment; 2-Regent Park Community Health Centre; 3-Canadian HIV Treatment Information Exchange; 4-Asian Community AIDS Services; 5-Women's College Hospital; 6-Ryerson University; 7-York University; 8-AIDS Bureau, MOHLTC

**Plain Language Summary:** Men who have sex with men (MSM) from ethno-racial communities face unique social and cultural challenges that affect their ability to effectively negotiate safer sex behaviors. A community based research project was carried out with frontline prevention workers and ethno-racial MSM to identify factors that affect risk taking behaviors and to identify future research directions. This presentation will share the preliminary findings emerging from the study and recommended areas for further research and evidence-based program planning.

**The Challenge:** The scarcity of research focusing on ethno-racial MSM hinders efforts to create a comprehensive evidence base for HIV prevention work in Ontario. To bridge this gap and to develop a community driven research agenda, a community based research study was developed by the AIDS Bureau Ethno-racial MSM Research Working Group. The objective of the study was to engage prevention workers and ethno-racial MSM to identify factors affecting risk taking behaviors and to identify research questions to better inform policy and practice for the target communities.

**Our Approach:** A qualitative study comprised of individual interviews with 10 prevention workers and 7 focus groups with MSM from the target communities. The study explored factors affecting risk behaviors, perceptions on the effectiveness of current interventions, and potential gaps in policies, programs and research. Results were analyzed thematically using N-Vivo and draft reports were developed to inform future research development.

**Key Findings:** Participants reported that ethno-racial MSM face unique social and cultural challenges that affect their ability to effectively negotiate safer sex behaviors. Social exclusion deeply impacts their identity, self-esteem, and efficacy in negotiating safer sex. Participants indicated that racism, homophobia, economic inequities, migration related challenges, and cultural and religious influences create a profound compounding impact on their sexual identities and relationships. The absence of personal experience with the loss and devastation of HIV foster denial and lessens the impact of prevention efforts. Further, stigma and discrimination against people with HIV (PHA) inhibits effective involvement of PHAs from ethno-racial communities, further contributing to their invisibility. Finally, participants reported that continued systemic inequities further hamper the effectiveness of many community based prevention efforts, especially amongst newcomers and youth from ethno-racial communities.

**Impact on Policy and Practice:** In order to be effective, HIV prevention efforts with ethno-racial MSM need to address the underlying social and cultural factors that affect these MSM. A comprehensive research agenda that explores the interplay between these social and cultural factors and systemic inequities will assist in further identifying vulnerabilities and resiliencies amongst these MSM, and will ensure evidence-based programs.

**Contact Information:** Alan Li, Tel: 416-364-2261, Email: alanli@sympatico.ca

## Clinical Science and Prevention

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**LUNG FUNCTION SCREENING WITH SPIROMETRY TO DETECT ASTHMA AND COPD IN PHAS**

Qu Cui [1]; Sue Carruthers [1]; Lynn Kelleher [1]; Fiona Smaill [1]; Marek Smieja [1]
1-McMaster University

**Plain Language Summary:** We studied 67 people living with HIV/AIDS (PHAs) at the Special Immunology Services (SIS) clinic at McMaster University and found that the majority of PHAs were at risk of future chronic obstructive pulmonary disease (COPD). We also found 4 previously undiagnosed cases of asthma or COPD. We recommended lung function screening of PHAs with chronic respiratory symptoms, or who smoke, for early detection of asthma and COPD.

**The Challenge:** Highly active antiretroviral treatment (HAART) has changed the disease pattern amongst PHAs. Chronic complications are playing a more important role in health care for PHAs contemporarily. Earlier detection and treatment of chronic respiratory diseases may improve quality of life for PHAs in the HAART era.

**Our Approach:** Consecutive consenting adult PHAs were recruited at the SIS clinic. FEV1 (forced expiratory volume in one second) and FVC (forced vital capacity) were measured by spirometry, followed by a self-administrated questionnaire and medical chart review. Global initiative for chronic Obstructive Lung Disease (GOLD) guidelines were used to diagnose COPD, and to classify PHAs at risk of COPD.

**Key Findings:** 67 PHAs participated. 48 (72%) were men. 50 (75%) were white. Mean (SD) age was 42.9 (9.3) years. 55 (82%) PHAs were on antiretroviral treatment. Mean CD4 was 515 (279) cells/L. 41 (61%) PHAs had viral load <50 copies/mL. Mean FEV1 was 3.3 (0.9) L. Mean FEV1 percent of age, gender, height and race predicted value (FEV1pp) was 91% (16%). Mean FVC was 4.3 (1.1) L. 34 (51%) PHAs with FEV1pp<90% were offered Ventolin testing, and 25 PHAs underwent post Ventolin spirometry. Mean improvement of FEV1 was 0.1 (0.2) L. 3 (5%) subjects were newly diagnosed asthma, in addition to 10 subjects who had a history of asthma. Women had 4.4 (95%CI: 1.2-16.4) times higher risk of asthma after controlling for the severity grade of breathlessness, and Beta for the grade of breathlessness was 2.2 (95% CI: 1.0-4.6). 39 PHAs were at risk of COPD. One subject had a history of emphysema, although this was not evident from his spirometry. One subject was diagnosed with moderate COPD. This 43 year old white male had previously smoked cigarettes for 22 pack-years and occasional marijuana for 10 years, and had a history of pneumonia and bronchitis.

**Impact on Policy and Practice:** We conclude that spirometry screening may improve detection of asthma and COPD amongst PHAs, and we recommend physicians regularly prescribe spirometry test for PHA population, especially for women, smokers, and those with respiratory symptom of breathlessness, in order to early detect and manage asthma and COPD.

**Contact Information:** Qu Cui, Tel: 905-522-8765, Email: cuiq2@mcmaster.ca

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**SISTERS, MOTHERS, DAUGHTERS AND AUNTIES: HIV VACCINE ACCEPTABILITY AMONG BLACK WOMEN IN TORONTO**

Peter A. Newman [1]; Charmaine Williams [1]; Notisha Massaquoi [2]; Carmen Logie [1]; Marsha Brown [1]
1-Faculty of Social Work, University of Toronto; 2-Women's Health in Women's Hands

**Plain Language Summary:** Canadian black women are disproportionately affected by HIV. HIV vaccines are one of the greatest hopes for controlling the epidemic; nevertheless, vaccine availability must occur in the context of acceptability and access to ensure the vaccine's effectiveness. We examined the acceptance of HIV vaccines among African and Caribbean black women.

**Objective:** To assess the acceptability of hypothetical HIV vaccines among black women in Toronto, and the impact of vaccine characteristics on acceptability.

**Methods:** We conducted a cross-sectional survey of 206 women of African and Caribbean descent recruited from community agencies in the Greater Toronto Area in 2006. 45-60-minute face-to-face interviews included a conjoint analysis experiment using a fractional factorial design to assess the acceptability of 8 hypothetical HIV vaccines with different attribute profiles: efficacy (99% vs. 50%), side effects (none vs. minor), cost ($10 vs. $250), duration of protection (10 years vs. 1 year), type of protection (cross-clade vs. single-clade), doses (1 vs. 4), and route of administration (oral vs. injection). We estimated the impact of each attribute on vaccine acceptability for each participant, and then averaged across participants using ANOVA. Self-administered questionnaires assessed HIV risk.

**Results:** Participants were 45% African, 49% Caribbean; mean age = 35 years (range 18-67 years). Median income was $13,344; 92% completed high school or greater. Most (81%) were born abroad, with an average of 18 years in Canada; 15% didn't hold Canadian citizenship or permanent residency. Two-thirds reported sexual activity in the past year, 72% of those with one partner; 11% (n=14) reported ≥3 partners. Perceived risks for HIV infection included: primary male partner/spouse (40%); obstacles in saying no to sex (45%); and risk of sexual assault (52%). 38% reported condom use during last sexual intercourse; 14% consistent condom use, past 12 months. Acceptability of 8 hypothetical HIV vaccines ranged from 25.9 (SD=29.2) to 79.4 (SD=28.4) on a 0-100 scale; mean acceptability = 55.5. Efficacy had the greatest impact (26.5; p<.001) on acceptability, followed by side effects (10.2; p<.001), cost (9.5; p<.001), and duration of protection (7.4; p<.001).

**Conclusions:** Moderate overall acceptability of HIV vaccines coupled with low acceptability of partial efficacy vaccines suggests HIV vaccine uptake is far from guaranteed among Canadian black women. Community education and social marketing to support the benefits of partial efficacy vaccines may be most effective in tandem with interventions to mitigate women's risks from primary partners and sexual violence, and government policies to guarantee access and affordability of HIV vaccines.

**Contact Information:** Peter Newman, Tel: 416-946-8611, Email: p.newman@utoronto.ca

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### ALTRUISTIC AND PROTECTION MOTIVATIONS AMONG VOLUNTEERS ENROLLED IN AN HIV VACCINE TRIAL

Peter A. Newman [1]; Charlene Cook [1]; Andrea Daley [1]; Lisa Kakinami [2]; William Cunningham [3]; Mona Loutfy [4]
1-Faculty of Social Work, University of Toronto; 2-Division of Public Health, University of Rochester, Rochester, New York, USA; 3-Division of General Internal Medicine and Health Services Research, UCLA, Los Angeles, California, USA; 4-Faculty of Medicine, University of Toronto

**Plain Language Summary:** The development of safe and efficacious preventive HIV vaccines is the greatest hope for controlling the AIDS epidemic; tens of thousands of volunteers at high risk for HIV infection will be needed to participate in HIV vaccine trials for the foreseeable future. Social-behavioral research is vital to ensure ongoing, safe and ethical HIV vaccine trial implementation.

**Objective:** To identify motivations for enrolling in an HIV vaccine trial among adults at high risk for HIV infection; and to assess the association between initial motivations and post-enrollment risk behaviors.

**Methods:** Volunteers enrolled in a Phase-IIb prophylactic HIV vaccine trial were invited to participate in a longitudinal socio-behavioural study. Trial selection criteria included: 18-45 years old; HIV-1 seronegative men and women; ≥2 sexual partners or unprotected anal sex in past 6 months. Participants completed confidential, self-administered baseline and 6-month questionnaires addressing demographics, motivations for trial enrollment and risk behaviors.

**Results:** Participants (n=48; >80% response rate) were predominantly male (98%) and gay or bisexual (96%). Overall, 85% were white, 10% Hispanic, 2% Asian, 2% Aboriginal. Mean age=37 years; average monthly income=$2011. At baseline, participants reported an average of 5 male sexual partners, past 30 days; 40% didn't use a condom for last anal sex; 17% rarely or never used condoms for anal sex. Motivations for enrolling in the trial were: 1) altruism (98% "to help end the AIDS epidemic"; 95% "to help my community"); 2) 73% perceived HIV risk; 3) 48% "to get extra protection against HIV" (protection motivation); 4) 46% "to get information about HIV vaccines"; 5) 19% "to get money"; and, 6) 15% "to protect my partner." Protection motivation at baseline was not associated with baseline risk behaviors, but was positively correlated with unprotected sex with primary (p=.04) and casual (p=.15) partners in the 6 months after joining the trial. Belief in ≥75% experimental vaccine efficacy at baseline was associated with unprotected anal sex at 6 months (p=.07).

**Conclusions:** HIV vaccine trial participants were primarily motivated by altruism and perceived HIV risk. Nevertheless, the positive association between protection motivation and unprotected anal sex subsequent to trial enrollment underscores risk associated with false beliefs in protection from an experimental vaccine in a placebo-controlled trial. Trial enrollment may be facilitated by appeals to altruism and to individuals who perceive HIV risk; however, clinical trial education among vulnerable communities and counselling to deter beliefs in "extra protection" are vital to the safe and ethical implementation of HIV vaccine trials.

**Contact Information:** Peter A. Newman, Tel: 416-946-8611, Email: p.newman@utoronto.ca

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### MEN AND WOMEN HAVE DIFFERENT GAPS IN KNOWLEDGE ABOUT HIV PREVENTION BEHAVIORS, MODES OF HIV TRANSMISSION, AND THE AVAILABILITY OF HIV TREATMENT OPTIONS

Julie Gosselin [6]; Louise Balfour [2,3,4,6]; Kim Corace [6]; John Kowal [1]; Giorgio A. Tasca [3,4,5,6]; Valerie Krysanski [6]; Lorraine Overduin [3,6]; Curtis L. Cooper [2,3,4]; Gary Garber [2,3,4]; Jonathan B. Angel [2,3,4]
1-Department of Psychology, The Ottawa Hospital Rehabilitation Centre; 2-Division of Infectious Diseases, The Ottawa Hospital-General Campus; 3-University of Ottawa; 4-Ottawa Health Research Institute; 5-Carleton University; 6-Department of Psychology, The Ottawa Hospital-General Campus

**Plain Language Summary:** HIV infection in humans is now pandemic. As of January 2006, the Joint United Nations Program on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) estimate that AIDS has killed more than 25 million people. Women are the fastest growing sub-group of people newly infected with HIV. There is growing concern about gender differences in HIV knowledge, in part because many heterosexual women still do not perceive themselves as an "at risk" group for HIV infection.

**Objective:** The main objective of this study was to examine gender differences in knowledge about HIV transmission and risk factors in several different medical and general population groups including HIV patients, Hepatitis C patients, and young college students. We also examined specifically HIV knowledge gaps in female respondents, in order to better inform future HIV prevention and education programmes aimed at this growing HIV population.

**Methods:** A total of 244 adult men and 108 adult women were recruited into this cross-sectional study, including HIV patients (n=155), HIV-hepatitis C co-infected patients (n=28), hepatitis C patients (n=89), and college students (n=80). Participants completed the Brief HIV Knowledge Questionnaire, which is a validated 18 item paper and pencil measure of general HIV Knowledge.

**Results:** Results indicate gender differences in the overall sample as well as in each population subgroup. When health behaviours were examined, we found that sexually active HCV patients were less likely to use a condom, than the other sub-group samples. Sexually active female respondents were less likely to use a condom than sexually active male respondents. These female respondents were also less likely to use a condom often or always than their male counterparts. When we compared HIV knowledge between male and female respondents, we found that male respondents answered more questions correctly than female respondents. Interestingly, each sample has their own specific knowledge gaps, confirming the need for more tailored HIV prevention and education programmes.

**Conclusions:** These results have important implications for clinical interventions aimed at increasing knowledge about HIV transmission and treatment in different population groups. The findings also suggest that ongoing HIV education for all HIV patients is needed but that additional, tailored educational interventions are needed to address important gaps in knowledge among women. The Brief HIV Knowledge Scale may be used as a clinical teaching tool to increase knowledge regarding transmission and self-protective behaviours.

**Contact Information:** Julie Gosselin, Tel: 819-737-8899 x78039, Email: jugosselin@ottawahospital.on.ca

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### INTERACTION OF HIV WITH THE GENITAL EPITHELIUM OF WOMEN

Aisha Nazli [1]; Charu Kaushic [1]
1-Dept of Pathology and Molecular Medicine, McMaster University

**Plain Language Summary:** Women now make up ~50% of new HIV-1 infections world wide. The consequence of these infections is much more severe in women. Much effort has been made to understand the pathogenesis of HIV in blood. However, HIV-1 is most widely spread by heterosexual transmission in women. Despite this, our basic understanding of how these viruses infect and spread in the female genital tract is rudimentary. Sexually transmitted viruses have different ways of infecting local cells present in the genital tract. In this study we examined the interaction of HIV with epithelial cells that line the genital tract of women.

**Objective:** To understand how HIV-1 interacts and causes infection in the female genital tract.

**Methods:** We utilized an ex-vivo genital tract primary cell culture model in which epithelial cells were isolated from different regions of female genital tract tissues and grown on transwells. The epithelial monolayers from vagina, cervix and endometrium were infected with X4 and R5 strains of HIV. Viral attachment was determined by HIV-GFP infection. HIV integration was measured by measuring pro-viral DNA by real time PCR. The productive infection was assessed by measuring viral RNA, P24 ELISA and infectious viral shedding detected on indicator cell line TZM-b1.

**Results:** We compared the susceptibility of the epithelial cells from different regions of genital tract and found that attachment and infection of HIV was higher in vaginal epithelial cells as compared to cervical and endometrial cells. P24 viral protein and infectious viral shedding was detected in all 3 tissues 24 hours post-infection. Overall the infection was quite low. Following apical infection, P24 viral proteins as well as the infectious viral particles were preferentially secreted into apical supernatants. 62-70 fold higher HIV-1 RNA was present in epithelial cells in presence of HIV-1 target cells compared to cultures that did not have target cells. Current studies are examining transcytosis of HIV-1 across epithelial monolayers.

**Conclusions:** HIV-1 may be utilizing multiple entry strategies to cause infection in female genital tract. It can directly infect primary genital epithelial cells, as seen in culture, but this infection does not appear to be very productive. Alternatively, HIV-1 may cross the epithelial cells by transcytosis. Understanding HIV-1 interaction with genital epithelium will allow us to design intervention strategies to prevent infection.

**Contact Information:** Aisha Nazli, Tel: 905-525-9140 x22589, Email: nazlia@mcmaster.ca

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### ADVERSE DRUG REACTION IN HUMAN IMMUNODEFICIENCY VIRUS-INFECTED INDIVIDUALS

Manuela Neuman [1,2]; Izabella Malkiewicz [1]; Norberto Krivoy [3]
1-In Vitro Drug Safety and BioTechnology; 2-Department of Pharmacology, University of Toronto; 3-Department of Medicine, Rambam Medical Centre, Haifa, Israel

**Plain Language Summary:** Patients infected with the human immunodeficiency virus (HIV) are at higher risk for adverse drug reactions than the HIV-negative population.

**The Challenge:** Drugs like antibiotics are needed to treat opportunistic infection. We aimed to validate the predictive and diagnostic value of the lymphocyte toxicity assay (LTA) for adverse drug reactions.

**Our Approach:** Patient lymphocytes were analyzed for toxicity to sulpha antibiotics (SMX). Of forty enrolled HIV patients, eighteen had SMX hypersensitivity syndrome reaction (HSR); ten tolerated the drug; and twelve had never received the drug.

**Key Findings:** When cases with HSR were compared with controls that tolerated the drugs, cytotoxicity was higher for cases: 33.2 ± 11.5 % versus 19.3 ± 9.0% for controls that did not presented the reactions ($p<0.05$).

**Impact on Policy and Practice:** Patient should be referred to the LTA before given an antibiotic to prevent such reactions.

**Contact Information:** Manuela Neuman, Tel: 416-673-6685, Email: manuela@sten.sunnybrook.utoronto.ca

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### RACIAL INFLUENCE ON LIPID PROFILE AT BASELINE AND FOLLOWING INITIATION OF HIV ANTIRETROVIRAL THERAPY

Curtis Cooper [1]; Jonathan Angel [1]
1-University of Ottawa, The Ottawa Hospital Division of Infectious Diseases

**Plain Language Summary:** Lipid abnormalities related to HIV drug therapy is currently of great concern. Analysis of our clinical database at The Ottawa Hospital indicates that race may influence lipid levels before the start of HIV therapy and may have an effect on the need for lipid lowering medications once HIV drugs are started. We hope to utilize the OHTN Cohort Study Database to study this question further.

**Objective:** Metabolic risk factors for cardiovascular disease differ by race. Hyperlipidemia is a recognized complication of HIV antiretroviral therapy. The interactions between race, HIV, antiretrovirals and lipids are not well-described.

**Methods:** Lipid data of patients initiating a first course of antiretroviral therapy at The Ottawa Hospital Immunodeficiency Clinic between January 1996 and February 2007 was evaluated using a SPSS 13.0 clinic database. Analysis was conducted by Student t-test, $\chi 2$, and linear regression. Mean values (mmol/L) and standard deviations (SD) are reported.

**Results:** 288 White and 118 Black patients was analyzed. Baseline total cholesterol and triglycerides were lower in Blacks. HDL was higher. This remained significant when controlled for factors influencing total cholesterol levels by univariate regression analysis (sex, HCV co-infection).

Table Baseline Lipids as Function of Race

| | Baseline Total Cholesterol | Baseline LDL | Baseline HDL | Baseline Triglycerides |
|---|---|---|---|---|
| White | 4.43 (1.16) | 2.55 (0.91) | 0.89 (0.29) | 2.32 (1.80) |
| Black | 4.19 (0.90) | 2.46 (1.12) | 0.99 (0.43) | 1.71 (1.54) |
| P Value | 0.05 | 0.55 | 0.02 | 0.001 |

Change in lipids from baseline did not differ by race at months 3, 6 or 12. The hyperlipidemic effects of protease inhibitor, d4T and NNRTI did not differ by race at these time points. A trend toward total cholesterol levels greater than 8.0 in Caucasians was noted at months 3, 6 , and 12 ( 5 to 9 % vs 2%). 6% of Caucasians and 1% Negros initiated lipid lowering therapy while on therapy (p=0.01). However, antiretroviral interruption for metabolic complications including hyperlipidemia did not differ by race (5% vs 4%, NS).

**Conclusions:** Overall, antiretroviral-related hyperlipidemia did not differ by race. However, higher use of lipid lowering therapy in Caucasians may be a consequence of higher baseline levels and/or a greater proportion developing very high total cholesterol levels on antiretroviral therapy. The mechanism(s) by which race may influence lipids and long-term cardiovascular disease risk in HIV disease merit further evaluation.

**Contact Information:** Curtis Cooper, Tel: 613-737-8924, Email: ccooper@ottawahospital.on.ca

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### THE CANADIAN HIV VACCINES PLAN AND COMMUNITY INVOLVEMENT

Shaleena Theophilus [1]; Kim Thomas [1]; Stephanie Nixon [2]
1-Canadian AIDS Society; 2-International AIDS Vaccine Initiative, New York, USA

**Plain Language Summary:** The hunt for a vaccine against HIV is still ongoing as it remains our best option for halting this epidemic. However, having an effective vaccine may take several years, and is dependent on the involvement of community members from across the globe. The Canadian HIV Vaccines Plan (CHVP) is a collaborative plan that outlines the key areas of involvement for researchers, governments and communities. This poster will give an overview of the CHVP, as well as strategies for community involvement outlined in the Plan.

**The Challenge:** In Canada, we have taken large steps into the search for a vaccine through the involvement of researchers in this area, by having community members come forward to take part in clinical trials, and recently through the Canadian HIV Vaccines Initiative. However, it was recognized that all sectors involved in the search for the HIV vaccine work together, drive and support each other in our efforts. As clinical trials will require the active involvement of communities including those most at risk for HIV, it was important that this plan articulate strategies for community engagement in vaccine development.

**Our Approach:** Through the recognition of the need for collaboration, Canada became one of the few industrialized countries to have created the Canadian HIV Vaccines Plan. This plan, created through collaboration between governments, researchers, and community, outlines Canada's contributions to the development of an HIV vaccine and articulates the vision for Canada's involvement at all levels.

**Key Findings:** Through the active engagement of key stakeholders in the community, a Community Engagement piece was created in the Canadian HIV Vaccines Plan. It outlines challenges for the general public, people living with HIV/AIDS, and community-based organizations, as well as strategies to overcome those challenges.

**Impact on Policy and Practice:** The Canadian HIV Vaccines Plan has already had an impact on Canadian Policy and Practice. The creation of the Canadian HIV Vaccines Initiative (CHVI) by the federal government is something that was outlined in this plan. The strategies outlined in the Canadian HIV Vaccines Plan would have a direct impact on the policies and practices for vaccine awareness and involvement by community members, as well as on the CHVI. Therefore, it is important that the strategies outlined in the Canadian HIV Vaccines Plan be disseminated broadly to all community members and agencies.

**Contact Information:** Shaleena Theophilus, Tel: 613-230-3580 x136, Email: shaleena@cdnaids.ca

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### EFFECTS OF EXERCISE IN WOMEN LIVING WITH HIV: WHAT THE RESEARCH DOES AND DOESN'T TELL US

Julie Hard [1]; Stephanie Nixon [2]; Kelly O'Brien [2]; Anne-Marie Tynan [1]; Richard Glazier [1,2]
1-Centre for Research on Inner City Health, The Keenan Research Centre in the Li Ka Shing Knowledge Institute of St. Michael's Hospital; 2-University of Toronto

**Plain Language Summary:** Exercise is generally accepted as important for health. But what do we know about the effects of exercise in women living with HIV? In general, the research suggests that exercise is safe and can help make adults with HIV stronger and more fit. However, these studies have mainly been conducted with men. Also, unique considerations for women living with HIV have not been explored. We describe these shortcomings to draw attention to this important area.

**Objective:** (1) To examine the effects of exercise on immunological, virological, cardiopulmonary, musculoskeletal, body composition and psychological outcomes in women living with HIV, and (2) to outline research directions to address knowledge gaps on the effects of exercise in women living with HIV.

**Methods:** This study involved a synthesis of research on exercise in women living with HIV, including systematic reviews, randomized controlled trials, and cohort studies to extrapolate data on immunological, cardiopulmonary, musculoskeletal, body compositional and psychological responses to exercise in men and women with HIV.

**Results:** Little research has exclusively investigated responses to exercise in women with HIV. However, outcomes have been reported for adults (primarily men) living with HIV. Meta-analyses of immunological and virological responses to exercise revealed no significant change in CD4 count or viral load between exercisers and non-exercisers, suggesting exercise is safe. Individual studies favour exercise for cardiopulmonary effects. In a small number of studies, women living with HIV demonstrated increases in muscular strength and increased muscle mass, which may alleviate wasting syndromes. Individual studies also reported improved mood states, depressive symptoms and perceptions of quality of life with exercise for people living with HIV. Results should be interpreted cautiously given small sample sizes, a limited number of female participants, and variability in study design.

**Conclusions:** There is a shortage of research that specifically describes responses to exercise for women living with HIV. Aerobic and progressive resistive exercise appear favourable for achieving cardiopulmonary, musculoskeletal, body compositional and psychological benefits without producing negative immunological consequences in adults with HIV; however, further research is needed to determine effects in women. Research should also take into account unique considerations pertaining to women, including metabolic and hormonal features, and differing social demands in the context of the lives of women living with HIV.

**Contact Information:** Julie Hard, Tel: 416-864-6060 x3452, Email: juliehard@gmail.com

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### DESIGN AND DEVELOPMENT OF A COMMUNITY RANDOMIZED CONTROL CLINICAL TRIAL OF MICRONUTRIENT & ANTIOXIDANT SUPPLEMENTATION IN PERSONS WITH UNTREATED HIV INFECTION: THE MAINTAIN STUDY

Neera Singhal [1]; D. William Cameron [1,2]
1-Ottawa Health Research Institute at the Ottawa Hospital, Clinical Epidemiology Program; 2-Department of Medicine, Division of Infectious Diseases, University of Ottawa

**Plain Language Summary:** Micronutrient deficiencies occur even in early HIV infection and increase risk of a poorer prognosis. Still, the role of micronutrient supplementation in medical management of HIV/AIDS is not clear. In this study, 200 consenting HIV infected persons, not taking or in need of anti-HIV drug treatment, will receive either a broad-spectrum micronutrient antioxidant supplement or identical appearing standard multivitamins and minerals. Study participants will be followed quarterly in clinic for two years. We expect that supplement recipients will have a slower decline in immune cells than those on standard multivitamins. Taking the supplement may safely delay start of indefinite, expensive and potentially toxic anti-HIV drug treatment.

**Objective:** To determine if a broad-spectrum micronutrient antioxidant supplement can safely delay CD4 cell decline in untreated HIV-infected persons compared to 100% recommended daily allowance (RDA) multivitamins and minerals.

**Methods:** A prospective, randomized, control, double blind clinical trial of supplementation of HIV positive adults currently not taking or needing ART with a broad-spectrum micronutrient antioxidant supplement or identical appearing RDA supplement, with quarterly follow up for change from baseline in absolute CD4 T lymphocyte count. Eligibility criteria: Consenting HIV infected adults with CD4+ cells 350-800 cells/mm3, HIV RNA <100,000 copies/mL, and not taking anti-HIV drugs in previous four months. Primary outcome: Change from baseline in absolute CD4 T lymphocyte count at 2 years. Secondary outcome: Time from baseline to start of anti-HIV drugs. Study location: Ontario and participating centres of Canadian HIV Trials Network (CTN). Study duration: Three years, one year for participant accrual and two years supplementation and follow up.
Statistical analysis: By intention to treat of all participants randomized. Three interim analyses are planned.

**Results:** We expect the supplement will be well tolerated and supplement recipients will have significantly higher absolute CD4 T lymphocyte count from baseline compared to controls.

**Conclusions:** We expect to conclude that the supplement delays decline in immunity and may safely delay start of expensive and potentially toxic anti-HIV drugs, with implications for health and health care savings. We hope that this well controlled clinical trial may instruct policy on reimbursement for micronutrient supplements to those with HIV and other oxidative stressor, malabsorptive and micronutrient-depleting conditions.

**Contact Information:** Neera Singhal, Tel: 613-737-8899 x71892, Email: nsinghal@ohri.ca

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### SOCIO-DEMOGRAPHIC FACTORS ASSOCIATED WITH CIRCUMCISION IN A COMMUNITY SAMPLE OF GAY AND BISEXUAL MEN IN ONTARIO

Kunyong Xu [1]; Ted Myers [1,2]; Dan Allman [1,2]; Liviana Calzavara [1,2]
1-HIV Social, Behavioural and Epidemiological Studies Unit, Faculty of Medicine, University of Toronto; 2-Department of Public Health Sciences, Faculty of Medicine, University of Toronto

**Plain Language Summary:** Socio-demographic factors associated with circumcision have not been studied. Our analysis suggests there are socio-demographic characteristics that are associated with circumcision. An understanding of these associations is important to consider when assessing the interplay between circumcision and HIV risk.

**The Challenge:** To describe the prevalence of self-reported circumcision among a community sample of gay/bisexual men in Ontario and to determine associated socio-demographic factors.

**Our Approach:** Data used for the analysis were from a study conducted among a community sample of self-identified gay or bisexual men in Ontario (n=5,080). Men completed a questionnaire which included questions on circumcision status and socio-demographic characteristics. Univariate and multivariate logistic regressions were used to identify factors that were associated with circumcision status.

**Key Findings:** The self-reported prevalence of circumcision was 64.8% (95% CI: 63.5% - 66.1%). Multivariate analysis showed that men living in the South Ontario were more likely to be circumcised compared those living in Toronto (AOR:1.38, p<0.0001). Men who were born in Canada were more likely to be circumcised than those born outside Canada (AOR: 1.98, p<0.0001). Men greater than 25 years old were more likely to be circumcised than younger men. (For men 25-39 AOR: 1.49, p<0.0001; For men 40-59 AOR: 1.56, p<0.0001). Compared to men whose first language was English, being circumcised was less likely for men whose first language was French (AOR: 0.50, p<0.0001), Chinese (AOR: 0.24, p<0.0001), Portuguese (AOR: 0.18, p<0.0001), Tamil (AOR: 0.07, p=0.0005), or Vietnamese (AOR: 0.45, p<0.0001). Men with college (AOR: 1.21, p=0.0218) or higher education (AOR: 1.39, p=0.0061) were more likely to be circumcised compared to those with high school or less education. Asian men (including East Asian, South Asian, Southeast Asian, and West Asian) were more likely to be circumcised compared to Caucasian men (AOR: 1.82, p=0.0002), while Latin American (AOR: 0.49, p=0.0253) and black men (AOR: 0.54, p<0.0024) were less likely to be circumcised.

**Impact on Policy and Practice:** The circumcision rate in this sample was high. However, circumcision reported in this analysis is lower than that reported in the United States and Australia. Because there may be an association between circumcision status and HIV risk (Calzavara et al 2007) understanding the prevalence of circumcision in this community sample is useful. These data show evidence that circumcision status on MSM in Ontario varies with factors such as age, first language, educational achievement and ethnicity. These understandings can be important both for predicting future changes in the epidemic as well as providing accurate information to men and their sexual partners. The high circumcision rate suggests that modification of circumcision practice may have limited impact and may raise crucial ethical issues.

**Contact Information:** Kunyong Xu, Tel: 416-836-5621, Email: kunyong.xu@utoronto.ca

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### IMPACT OF VIRAL LOAD ON THE HUMORAL RESPONSE IN HAART TREATED CHILDREN

Sylvie Faucher [1]; Alice Sherring [1]; Dragica Bogdanovic [1]; Michèle Bergeron [1]; Paul Sandstrom [1]; Ampha Kammy [2]; Johanne Samson [2]; Normand Lapointe [2]; Francis Mandy [1]
1-National HIV and Retrovirology Laboratories, Public Health Agency of Canada; 2-Centre Maternel et Infantile sur le SIDA, Hospital Ste-Justine, Montréal

**Plain Language Summary:** The impact of a prolong suppression of viral load on the evolution of HIV antibody levels was studied in HAART treated children for a period of 16 months. The study showed that patients with suppressed viral load showed a decline of HIV antibodies detectable at 8 months post-treatment. No change in antibody avidities or levels of CMV and EBVantibodies were detected during the study period.

**Objective:** Establish the impact of viral load on antibody levels and avidity maturation among HAART treated children with controlled (group I) and uncontrolled viral load (group II).

**Methods:** Antibody end point titers and avidity to 11 HIV-1 proteins, CMV and EBV lysates were determined from 12 HAART treated children during a period of 16 months. Plasma samples were incubated with a mix of 13 protein-coupled fluorescent beads (Luminex) and detection was performed with anti-human IgG-biotin and Streptavidin-PE. Antibody avidity was determined from the residual titer measured when antibodies were incubated in presence of a chaotropic agent.

**Results:** High HIV-1 antibody titers were detected in both groups of patients with a predominant response towards env and gap/pol proteins. Antibodies to the matrix protein p17 were detected in only 9/12 patients with titers 1-3 log lower than other gag antibodies. Among the regulatory proteins, nef and tat antibodies were the most frequently detected (75%). Antibodies to HIV declined in group I with an average of 0.2-0.3 log reduction of anti-env and anti-nef antibodies at 8 months and 0.2-0.6 log at 16 month post-treatment. In group II, antibody levels were maintained or increased overtime. Antibody avidity and antibody titers to CMV and EBV were comparable in both groups and remained unchanged during the study period.

**Conclusions:** A multiplex analysis of HIV, CMV and EBV antibodies demonstrated a decline of HIV antibodies but no change in antibody levels to ubiquitous infections in HAART treated children with prolong suppression of viral load. This study also showed the lack of impact of viral load on the evolution of antibody avidity during treatment.

**Contact Information:** Sylvie Faucher, Tel: 613-941-8855, Email: sylvie_faucher@phac-aspc.gc.ca

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**EFFECT OF ANTIRETROVIRAL DRUG REGIMENS ON SUPPRESSION OF GENITAL VIRAL LOADS IN HIV-INFECTED WOMEN WITH SUPPRESSED PLASMA VIRAL LOAD.**

Allyson Ion [4]; Sameer Kassim; Charu Kaushic [3]; Sonya Buracond; Lynn Kelleher [4]; Fiona Smaill [1,4]; Philippe El-Helou [4,5]; Marek Smieja [1,2,4]
1-Department of Pathology and Molecular Medicine, McMaster University; 2-Department of Clinical Epidemiology and Biostatistics, McMaster University; 3-Centre for Gene Therapeutics, McMaster University; 4-Special Immunology Services Clinic, McMaster University Medical Centre; 5-Department of Medicine, McMaster University

**Plain Language Summary:** A suppressed plasma viral load is the primary endpoint of antiretroviral therapy, and a powerful predictor of good clinical outcome. Studies have suggested viral compartmentalization resulting in a persistent and detectable viral reservoir in the genital mucosa, even if virus is suppressed in plasma. Recent data suggest that vaginal drug levels of certain anti-retrovirals, such as efavirenz or protease inhibitors, may be sub-optimal, but there are no data on genital tract viral load suppression by drug regimen. Our study found measurable genital tract HIV in 4 of 13 women with fully suppressed plasma viral load, with no difference between NNRTI- and PI-based HAART regimens.

**The Challenge:** To compare the effect of PI-based and NNRTI-based HAART regimens on cervical and vaginal viral loads in HIV-infected women with undetectable plasma viral load.

**Our Approach:** Blood plasma samples were obtained during routine blood draw from adult female patients at the HIV clinic in Hamilton. Genital tract samples were obtained from consenting study participants during a regularly scheduled physical exam. Plasma, cervical and vaginal viral loads were determined with an HIV quantitative assay previously standardized in blood plasma and genital secretions. Current HAART regimen was abstracted from chart review. Descriptive statistics and cross-tabulations were analyzed using SPSS version 15.0.

**Key Findings:** HIV-infected Canadian-born (48.1%) and non-Canadian-born (51.9%) women (n=27) with a mean age of 40.4 years (±9.4) and black (51.8%) and white (44.4%) ethnicities had an overall mean cervical and vaginal load of 2.52 log copies/ml and 2.78 log copies/ml, respectively. 17 out of the 27 (63%) women were on HAART, 13 of whom (76.5%) had an undetectable plasma viral load. Five women were on a NNRTI-based HAART regimen (29.4%) and twelve women were on a PI-based HAART regimen (70.6%). None of the women were on Trizivir. Women on a NNRTI-based regimen had mean cervical and vaginal viral loads of 2.24 and 1.89 log copies/ml respectively whereas women on a PI-based regimen had mean cervical and vaginal viral loads of 2.77 and 3.02 log copies/ml respectively, however these differences were not statistically significant. One out of four women (25%) had a detectable cervical viral load with a NNRTI-based HAART regimen, but undetectable plasma and vaginal viral loads. Out of the women on a PI-based regimen with undetectable plasma viral load, three out of nine (33.3%) had a detectable cervical viral load and two out of nine (22.2%) had a detectable vaginal viral load. Although this analysis suggests that women are more virally suppressed on a NNRTI-based regimen, the differences between regimens were not statistically significant. This study does highlight, however, that even with undetectable plasma virus, HIV may be detectable in the genital tract.

**Impact on Policy and Practice:** HIV virus is detectable in vaginal and cervical fluid of women who are fully suppressed on HAART therapy, and both NNRTI-based and PI-based regimens may be associated with detectable genital viral load. These findings emphasize the need to study and optimize drug regimens, which will fully suppress virus in the genital tract, and to continue to counsel women to maintain safer sex practices regardless of HAART therapy.

**Contact Information:** Allyson Ion, Tel: 519-443-7573, Email: allysonion@hotmail.com

## Research Tools and Methods

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**IMPLEMENTING RESPONDENT DRIVEN SAMPLING: LESSONS LEARNED**

Sue McWilliam [1]; Lynne Leonard [1]; Emily De Rubeis [1]; Aideen Reynolds [1]
1-HIV Prevention Research Team, University of Ottawa

**Plain Language Summary:** This paper reports on the use of respondent driven sampling (RDS) as a recruitment methodology to sample women and men who inject drugs in Ottawa. The major objectives of our study were to collect data, via interviews and dried blood samples, to identify and characterize potential distinct networks of injection drug users (IDUs) and determine routes by which HIV and hepatitis C (HCV) are being transmitted. This information will be used to identify HIV and HCV infection clusters and strains, confirm social network data, and provide a basis for primary and secondary prevention interventions.

**The Challenge:** Implementing RDS uncovered a variety of logistical challenges. RDS is similar to snowball sampling as it involves peer, chain referral sampling, but has a built in mathematical system that calculates selection probabilities. Participants recruit their peers and the research team tracks who recruited whom to create a resulting model that enables researchers to provide population estimates and measure the precision of their estimates. RDS is particularly suited to research with groups that are small, inaccessible, and marginalized (1).

**Our Approach:** We began by recruiting a group of 8 first generation "seed" participants, who were referred by local service providers. The seeds were selected based on their perceived 'connectedness' within the community and represented a diversified cross-section of the IDU population in Ottawa. Once interviewed, each participant was given 3 recruitment cards to pass on to their injection drug using peers. Our aim is to recruit 400 participants over 3 months using 6 interviewers.

**Key Findings:** The findings provide useful information for improving RDS field techniques and measuring the effectiveness of this sampling method. Identifying connected seeds, stressing the importance of peer referral and talking to participants about their experiences in the study, helped identify logistical challenges in a timely manner.

**Impact on Policy and Practice:** The added utility of applying this methodology apart from its direct relevance to the research question of characterizing social networks is that we will arrive at HCV and HIV prevalence rates that will have greater generalisability or external validity as they will have been derived from IDUs beyond those accessible at the more usual recruitment sites. In addition, through applying RDS, the research process may also have a prevention intervention effect in that IDUs who present for interview may well be those that are unaware of, or previously have not accessed, the range of harm reduction resources available in our city.

**Contact Information:** Sue McWilliam, Tel: 613-562-5800 x8277, Email: smcwilli@uottawa.ca

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**SCOPING STUDIES AS A METHOD TO INFORM GUIDING PRINCIPLES FOR THE DEVELOPMENT OF BEST PRACTICE GUIDELINES: AN EXAMPLE FROM THE FIELD OF HIV AND REHABILITATION**

Annette Wilkins [1]; Kelly O'Brien [1,2]; Elisse Zack [1]; Patty Solomon [3]
1-Canadian Working Group on HIV and Rehabilitation; 2-Department of Physical Therapy, University of Toronto; 3-School of Rehabilitation Science, McMaster University

**Plain Language Summary:** We describe using a scoping study (a research method that includes a literature review and consultation phase) to identify recommendations for the development of best practice guidelines in the area of HIV and rehabilitation. The literature review highlighted a need to further develop research, clinical practice, and policy for HIV rehabilitation, in order to address the range of impairments, activity limitations, and participation restrictions experienced by people living with HIV (PHAs).

**The Challenge:** To describe scoping study methodology used to inform the future development of best practice guidelines for rehabilitation in the context of HIV.

**Our Approach:** The scoping study consisted of two phases. Phase One included a review of published and grey literature on HIV and rehabilitation from databases including MEDLINE, EMBASE, CINAHL and PsychINFO. Literature was classified using the Episodic Disability Framework and content from key articles further categorized as addressing HIV-related disability, interventions, and roles of rehabilitation professionals. Phase Two included a series of focus groups and interviews with a range of stakeholders. We report findings for Phase One.

**Key Findings:** Of the 4274 identified abstracts, 1260 from MEDLINE were reviewed. Of these, 615 abstracts addressed elements of the Episodic Disability Framework and 146 were identified as key articles for further review. From the key articles, 62% (91/146) were published after the introduction of highly active antiretroviral therapy (HAART) in 1996. Fifty-eight articles (40%) addressed disablement needs of PHAs, 43% addressed interventions, and 17% addressed roles of rehabilitation professionals in HIV care. Despite increasing literature in this field, there is a need to further evidence the role and effect of rehabilitation interventions in the post-HAART era. In conclusion, scoping studies offer a comprehensive approach for exploring guiding principles for best practice guidelines development. Advantages of this approach include its systematic procedure, broad inclusion criteria, and consultative phase. Collectively this methodology will help the future development of best practice guidelines in rehabilitation in the context of HIV.

**Impact on Policy and Practice:** People living with HIV may be living with impairments, activity limitations and participation restrictions due to HIV or its associated treatments; hence there is an increasing role for rehabilitation. Identifying key principles for the development of best practice guidelines in HIV and rehabilitation will advance future practice and policy to ensure that PHAs may access and receive optimal rehabilitation care, treatment and support.

**Contact Information:** Kelly O'Brien, Tel: 416-978-0565, Email: kelly.obrien@utoronto.ca

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### HOW DO EXISTING HIV-SPECIFIC INSTRUMENTS MEASURE UP? EVALUATING THE ABILITY OF INSTRUMENTS TO DESCRIBE DISABILITY EXPERIENCED BY ADULTS LIVING WITH HIV

Kelly O'Brien [1,2]; Ahmed M. Bayoumi [1,2]; Carol Strike [3,4]; Nancy L. Young [2,5]; Ken King [6]; Aileen M. Davis [2,7]
1-Centre for Research on Inner City Health, St. Michael's Hospital; 2-Department of Health Policy, Management and Evaluation, University of Toronto; 3-Centre for Addiction and Mental Health; 4-Department of Psychiatry, University of Toronto; 5-School of Human Kinetics, Laurentian University; 6-Canadian Working Group on HIV and Rehabilitation; 7-University Health Network, Toronto Western Hospital

**Plain Language Summary:** We reviewed existing HIV-specific questionnaires to see how well they captured four major dimensions of disability within the Episodic Disability Framework, a framework developed from the perspective of adults living with HIV. Of the 30 questionnaires that met the inclusion criteria, symptoms/impairments and difficulties with day-to-day activities were the dimensions captured in greatest depth while uncertainty and challenges to social inclusion were the least well described. These instruments provide a foundation to build a measure of disability for adults living with HIV.

**The Challenge:** To evaluate how well existing HIV-specific health-status instruments capture the experience of disability for adults living with HIV.

**Our Approach:** We assessed the content validity of existing HIV-specific instruments for their ability to describe disability as defined by the Episodic Disability Framework. We developed this framework to conceptualize the disability experience from the perspective of adults living with HIV. We searched databases from 1980 to early 2006 for English language, HIV-specific, self-reported questionnaires, that had been tested for reliability and validity. We conducted a formal document analysis matching items of the instruments with components of the framework. Instruments were specifically evaluated for their ability to capture major dimensions of disability in our framework.

**Key Findings:** We reviewed 4274 abstracts, from which 30 instruments met the inclusion criteria and were retrieved. Instruments measured 10 different health-related concepts, and ranged from 9-177 items. Of the 4 major dimensions of disability in our framework, symptoms/impairments were included in all instruments, difficulties with day-to-day activities and challenges to social inclusion in 16, and uncertainty in 9. Seven instruments contained at least 1 item from all 4 dimensions of disability, 5 of which were developed after combination antiretroviral therapy became standard. In general, symptoms/impairments and difficulties with day-to-day activities were the disability dimensions characterized in greatest depth while uncertainty and challenges to social inclusion were the least well described.

**Impact on Policy and Practice:** Although none of the instruments evaluated in this study captured the full spectrum of disability as conceptualized by the Episodic Disability Framework, these instruments provide a foundation from which to build a measure of disability for adults living with HIV. A future instrument may be used by health providers and policy makers interested in measuring the prevalence and impact of disability experienced adults living with HIV.

**Contact Information:** Kelly O'Brien, Tel: 416-978-0565, Email: kelly.obrien@utoronto.ca

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### A QUALITATIVE EVALUATION MODEL: A CASE STUDY OF AIDS NIAGARA

Leonard Kooperman [1]; Phil Durrant [2]; Livia Martin [1]
1-AIDS Niagara; 2-Niagara College

**Plain Language Summary:** This research designed and implemented a qualitative evaluation model for the purpose of evaluating AIDS Niagara. The project developed a questionnaire toward capturing Knowledge, Attitudes, Beliefs and Behaviors of clients. Strengths, Weaknesses, Opportunities and Threats were explored through nominal group techniques with Staff, clients the Board and community partners. The project was a partnership between AIDS Niagara and Niagara College and included student interns from the Social Service Worker Program of Niagara College assisting with the questionnaires, interviews and group processes. AIDS Niagara Staff were integrated into the research project at every critical juncture toward increasing the capacity of the agency to continuous self-evaluation and continuous quality improvement. The final document can be considered a "toolkit" and available to other AIDS Service Organization and non-profit organizations. This will allow the replication of the evaluation techniques employed by this project.

**The Challenge:** To develop and organize nominal groups for key stakeholders, The Board, the Staff, clients and community partners. To develop a KABB for clients and identify and recruit clients as respondents for the survey. To train the student interns in group process and interviewing techniques.

**Our Approach:** The research team incorporated the AIDS Niagara Staff in the various aspects of the research project in order to familiarize them with the process for future evaluations. We shared our finding with all the participants including the Board, Staff, clients and community partners. An overall inclusiveness pervaded the entire project. Often non-profit organizations rely on intuition and past practices to develop themselves and their organization. This kind of systematic evaluation provides factual feedback toward adjusting services, changing services or keeping their services at a status quo.

**Key Findings:** Three major challenges emerged from the research: the lack of optimum levels of government funding, the social isolation of clients and client accessibility to health services and other social services. The three challenges will be discussed in detail together with opportunities for meeting these challenges.

**Impact on Policy and Practice:** The finding provide many opportunities and specific ways in which both the government in general and AIDS Niagara can meet these challenges. The research project puts in place specific ways to meet these opportunities.

**Contact Information:** Leonard Kooperman, Tel: 905-321-1383, Email: lenkooperman@aol.com

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### DEVELOPMENT OF AN HIV TREATMENT OPTIMISM SCALE FOR HIV-POSITIVE GAY AND BISEXUAL MEN

David Brennan [1]
1-Factor-Inwentash Faculty of Social Work, University of Toronto

**Plain Language Summary:** Since the introduction of combination drug therapy in 1997, HIV prevention experts have expressed concern that optimistic beliefs about HIV treatment might increase sexual risk. This study was designed to create a measurement tool to assess Treatment Optimism among high-risk HIV-positive gay and bisexual men (GBM) currently on HIV treatment. A single instrument was not supported by this analysis. Instead, three separate scales were supported. These scales measure beliefs about the transmissibility of HIV, quality of life and motivation to use condoms.

**Objective:** To develop a reliable measure of HIV treatment optimism among HIV-positive gay and bisexual men (GBM) who are currently on treatment.

**Methods:** Potential items to be included in an HIV Treatment Optimism scale were reviewed by 17 HIV-positive GBM, resulting in a 21-item instrument. After pilot testing, data were collected from a multi-city sample of high-risk HIV-positive GBM (n= 303), who were currently on treatment and were recruited to attend a two-day sexual health seminar. The scale items were analyzed utilizing Principal Components Analysis (PCA) and reliability testing.

**Results:** The factor analysis resulted in the development of three separate scales. The Susceptibility scale contained 10 items associated with a belief that HIV is less transmissible while on HIV treatment. The Condom Motivation scale contained 5 items addressing a decreased motivation to use condoms while on treatment and the Severity scale contained 4 items associated with a decreased sense of the severity of an HIV diagnosis. Reliability coefficients (α) and mean inter-item correlations (M) for the three scales were acceptable (Susceptibility, α = .86, M = .39; Condom Motivation, α = .84, M = .50; Severity, α = .71, M = .37). Combined as one scale, the reliability coefficient was respectable (α = .76), but the mean inter-item correlation was .14. Based on this analysis, use of a single measure was not supported and three separate scales were developed.

**Conclusions:** The use of one scale to measure treatment optimism among HIV-positive GBM was not supported. Three separate scales addressing beliefs about the transmissibility of HIV while on treatment (Susceptibility), the quality of life while on HIV treatment (Severity) and the motivation to use condoms consistently while on treatment (Condom Motivation) may be better markers for assessing optimistic beliefs about HIV treatment. The use of these scales may be beneficial in assessing the extent to which HIV treatment optimism is a salient issue in sexual risk reduction among HIV-positive GBM.

**Contact Information:** David Brennan, Tel: 416-978-3273, Email: david.brennan@utoronto.ca

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### EFFECTIVENESS OF COMMUNITY OUTREACH AND RECRUITMENT EFFORTS FOR POPULATION-BASED STUDIES: EXPERIENCES OF THE EAST AFRICAN STUDY IN TORONTO (EAST)

Kimberly Gray [1]; Wangari Tharao [2]; Liviana Calzavara [1,3]; Ann Burchell [4]; Ted Myers [1,3]; Robert Remis [3]; Catherine Chalin [3]; Jane Polsky [1]
1-HIV Social, Behavioural and Epidemiological Studies Unit, University of Toronto; 2-Women's Health in Women's Hands; 3-Department of Public Health Sciences, University of Toronto; 4-Division of Cancer Epidemiology, McGill University; 5-Ontario Ministry of Health and Long Term Care, HIV Laboratory

**Plain Language Summary:** We evaluated our recruitment efforts from EAST, a study addressing HIV in communities from East African countries. Our results show that successful recruitment requires ongoing and direct contact with community members through a wide range of recruiters, events, and public venues. Efficient systems are imperative to track potential participants and evaluate recruitment efforts.

**The Challenge:** Our purpose was to address gaps in research concerning the successful engagement of communities from countries where HIV is endemic through the systematic tracking of community participation and assessing the effectiveness of recruitment efforts.

**Our Approach:** Tailor made recruitment strategies involving these highly dispersed communities were developed. Two mechanisms were used to build the sampling frame: 1) direct approach (via 40 recruiters) at community events, public venues, and organizations and through snowballing and 2) third-party lists from community organizations. Detailed recruitment and communication information was collected. Univariate and bivariate analyses were used to describe and analyze modes of recruitment, recruitment outcomes, number of contacts made, length of time until outcome, and reasons for non-participation.

**Key Findings:** A sampling frame of 1570 individuals was generated during the study. The majority of individuals (62%) were approached through snowballing or direct contact and 10% through third-party lists. Those who were directly recruited were more likely to be interviewed compared to those from lists (29% vs 19%, p=0.008). Of the 1497 eligible individuals, 29% participated and 47% were unreachable. Once individuals were contacted, 16% refused. The most cited reasons for refusing were ‘too busy’ (44%) and ‘not interested’ (36%). Women were more likely to refuse (10% vs 5% p=0.0004). 7317 calls to participants were documented. The average number of calls per person was 5.5 (range 1-49), with 25% of individuals called 7+ times. On average it took 4.2 weeks to secure an interview (range 0-63) and 10 weeks for a refusal (range 0-96).

**Impact on Policy and Practice:** Direct contact, through recruiters or snowballing, was the most effective mode of reaching community members. Although we were unable to successfully contact over half of the sampling frame, the refusal rate was low. Further research is needed to address the higher refusal rate in women. Efficient systems and diligent recording were necessary to manage the large volume of calls and length of time required to secure an outcome. This evaluation is highly relevant for future studies with these communities and will be used to inform the development of surveillance efforts such as E-Track.

**Contact Information:** Kimberly Gray, Tel: 416-946-7026, Email: kimberly.gray@utoronto.ca

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### SUBJECT TERMINOLOGY AT THE AIDS COMMITTEE OF TORONTO LIBRARY AND THE CHANGING NATURE OF THE HIV/AIDS COMMUNITY

Erica Lee [1]
1-AIDS Committee of Toronto

**Plain Language Summary:** The AIDS Committee of Toronto (ACT) Library is one of the largest publicly-accessible HIV/AIDS libraries in North America. In 2006 the ACT Library published the second edition of its "HIV/AIDS Thesaurus". The thesaurus is the list of subject terms the library uses to describe the books, articles and other resources in the library collection. A terminology update was needed to reflect changes in the library collection since the thesaurus was first published in 2000, changes that have been impacted by broader changes in the HIV/AIDS community. A comparison between the different versions of the thesaurus in use between 2000 and 2006 and a look at the thesaurus review process provide an interesting illustration of the factors that have impacted the changing face of the HIV/AIDS epidemic in recent years.

**Objective:** To update the ACT Library's "HIV/AIDS Thesaurus" so that the terminology better reflects the current nature of the ACT Library collection and the changing needs of library users.

**Methods:** The original thesaurus, completed in 2000, and an expanded version of the thesaurus, developed in 2002, were reviewed term by term, then merged and updated. Terminology choices took into consideration factors including: the changing nature of HIV from a terminal to a chronic condition; improvements in the understanding of HIV infection since the early days of the epidemic; new strategies and challenges in the fight against HIV/AIDS; and the changing use of the ACT Library, the library collection, and program delivery at ACT.

**Results:** The second edition of the "HIV/AIDS Thesaurus" was published in 2006 and adopted as the new subject standard for the ACT Library, with over 130 new terms added. Copies of the thesaurus were offered and distributed to interested organizations and individuals. Web pages on the ACT website were also created to support the online use of the thesaurus by the public.

**Conclusions:** The thesaurus review process undertaken by the ACT Library highlights in a unique way some of the broader changes that have occurred in the HIV/AIDS community in recent years in terms of living with HIV/AIDS and the delivery of HIV/AIDS-related services.

**Contact Information:** Erica Lee, Tel: 416-340-8484, x303, Email: elee@actoronto.org

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### NEW METHODS FOR IMPROVING THE VALIDITY OF STUDIES OF MARGINALIZED COMMUNITIES AND HIDDEN POPULATIONS: RESPONDENT-DRIVEN SAMPLING AND TIME-LOCATION SAMPLING

Greta Bauer [1]
1-Epidemiology & Biostatistics, The University of Western Ontario

**Plain Language Summary:** Commonly used statistical methods are based on the assumption that data come from random samples of the populations or communities of interest. In HIV research, this is often not the case, as some communities are “hidden” and not enumerable due to social stigma, invisibility, immigration status, or legality of behaviours. Thus, researchers often rely on ‘convenience’ methods such as venue-based samples, grab samples or snowball samples, all of which are considered to have methodological weaknesses that can seriously limit the credibility of conclusions. This has implications for reaching hidden and high risk populations and understanding and addressing their needs. Recently developed methods for sampling and analysis provide probability-based improvements that allow for more rigorous design of studies involving marginalized or hidden groups.

**The Challenge:** To identify methods to improve the validity of studies of hidden populations.

**Our Approach:** Review of methods literature to identify recently developed methods for improving the validity of study designs for marginalized communities.

**Key Findings:** Two promising new methods were identified. 1) Respondent-driven sampling (RDS) uses social networks for recruitment, similar to a snowball sample. However, recruitment patterns are tracked to provide additional information needed to attach recruitment probabilities to participants and allow for calculation of accurate variances in statistical analysis. 2) Time-location sampling (TLS) is a venue-based recruitment technique that involves an initial phase of assessment to construct sampling units and account for the probability of attendance at venues. Both RDS and TLS produce results with higher validity than their respective convenience sample parallels, as selection bias is reduced, information bias may be reduced, and appropriate statistics can be calculated. The processes to implement both methods require community involvement and investment, and can function to build both trust and capacity.

**Impact on Policy and Practice:** Where policy and practice are based on research evidence, these newer methods provide an opportunity to produce evidence that is more rigorous and will better withstand scrutiny. This presents an advantage especially for communities or issues where stigma or misconceptions produce a lack of political will and a tendency to discount the results of research. Moreover, both methods are highly appropriate for community-based research.

**Contact Information:** Greta Bauer, Tel: 519-661-2111 x86262, Email: greta.bauer@schulich.uwo.ca

## Service Delivery and Peer Support

### 271

**CHOICES: PEER SUPPORT FOR PEOPLE CO-INFECTED WITH HIV/HCV**

Colleen Price [1]; Adriana Carvalhal [2]
1-Choices Peer Support Group; 2-Department of Psychiatry & Behavioural Neuroscience, McMaster University

**Plain Language Summary:** A peer support group for people who are co-infected with HIV and Hepatitis C Virus (PLHIV/HCV) called Choices was developed and examined with a low cost, preliminary evaluation. Results showed high program participation and several indicators of positive health, harm reduction and psychosocial outcomes.

**The Challenge:** PLHIV/HCV face many challenges including: high risk for addictive and other co-occurring mental disorders, significant barriers to accessing appropriate treatment including stigma issues, and challenges adhering to medication regimens. As a result of these and other challenges engaging this population in appropriate treatment, health education and other support is very difficult. Although peer-based approaches holds promise in reaching this population funding support for program development and evaluation has been difficult to obtain.

**Our Approach:** The objective of "Choices" is to provide a safe, non-stigmatizing environment for PLHIV/HCV to share their experiences and receive support around the "double trouble" of HIV and HCV. The group meets weekly and the focus of each session is to optimize mental and physical health through education, wellness promotion, prevention and referrals for support. The model includes group discussion facilitated by a trained peer as well as health education delivered by health professionals such as HIV/HCV physicians, treatment nurses and addiction specialists. Addiction is an important focus and supports in this area are based on a harm reduction model consistent with best practices. Medication adherence and strategies to increase taking medication on time are also critical program ingredients.

**Key Findings:** The program has successfully engaged a core group of five PLHIV/HCV (2 female and 3 male) supplemented occasionally by "drop-ins". Regular weekly participation has been high and qualitative evidence of health and individualized psychosocial outcomes is positive. This includes, for example, successful housing for one person; abstinence from alcohol for another; agreement to take the HIV meds by another; and transition off needles by another. High value was placed by participants on the non-stigmatizing peer support. Education sessions were preferred over open discussion only. Health professionals continue to participate on a voluntary basis.

**Impact on Policy and Practice:** It is too early to identify policy or program-level impact. Early findings suggest, however, a high potential for such impact pending more rigorous evaluation. Funding is needed to support the program itself as well as its more formal evaluation.

**Contact Information:** Adriana Carvalhal, Tel: 905-521-2100 x75998, Email: carvalh@mcmaster.ca

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**TODAY: IT IS TIME TO RECLASSIFY HIV**

Jake Peters [1]
1-Community Member, Toronto, Canada

**Plain Language Summary:** Today: A person can enjoy stable health with fully repressed HIV provided one has appropriate antiviral medication. In light of this, prohibitions limiting travel and immigration as well as other barriers restricting normal rights of a person living with HIV should be abolished.

**The Challenge:** Today: Medical treatments have evolved to the degree that HIV is a manageable, treatable, survivable condition. Today: HIV is no more infectious than Hepatitis, however, legislation views HIV through the eyes of yesterday. Today: More than 104 countries* impose restrictions and barriers on people living with HIV. Today's challenge is to grab restrictive legislation by the scruff of the neck and bring it up to date. Today: It is time to reclassify HIV. *European AIDS Treatment Group, Sept. 2007

**Our Approach:** Today: Using evidence based on good medical treatment and practice, we can demonstrate that HIV, coupled with access to treatment, is no longer the threat to life it was two decades ago. Comparing morbidity from the period before HAART** to today, we can show that legislation needs to be updated to reflect this reality. Today: It is denial and ignorance, coupled with the absence of antiretroviral therapy and healthcare that are to be feared. **Highly Active Anti Retroviral Therapy

**Key Findings:** Today: People with HIV can achieve stable health with currently available antiviral medications. Prejudicial suffering and cruelties that compound the burden of people living with HIV are unnecessary penalties amplified by inappropriate and obsolete HIV legislation.

**Impact on Policy and Practice:** Enhanced quality of life of people living with HIV and of Global Society will result from an enlightened reclassification of HIV, access to antiviral medications and abolition of discriminatory legislation today.

**Contact Information:** Jake Peters, Tel: 416-323-1177, Email: jakepeters@rogers.com

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### TWO APPROACHES TO PROVIDING HIV SERVICES IN THE COMMUNITY TO PHAS: A CASE MANAGEMENT MODEL

Adriana Carvalhal [1]; Tom Hammond [2]; Robin Weir [3]; Gina Browne [3]; Jacqueline Roberts [3]; Amiram Gafni [3]
1-Department of Psychiatry & Behavioural Neuroscience, McMaster University; 2-AIDS Committee of Guelph; 3-Community-linked Evaluation AIDS Resource (CLEAR) Unit, McMaster University

**Plain Language Summary:** A diagnosis of HIV can carry with it tremendous social stigma. People living with HIV/AIDS (PHA) face not only a chronic illness and complex medical demands but also extensive social challenges; they have various service needs: these can include health care, financial assistance, emotional and mental health support, assistance with daily activities, drug treatment, housing, and family services. On-demand health and social services that address single problems or risk factors are less effective and more expensive than proactive and comprehensive services. The case management model is an alternative to approach often fragmented services. There is some literature to support that case management interventions can reduce costs of HIV treatment, and improve the economic, social, physical, and emotional well-being of HIV-infected persons.

**Objective:** The purpose of this pilot study was to assess the impact of strength-based proactive case management approach to PHA care on the improvement in PHA satisfaction with HIV services, compliance with medications, quality of life and psychiatric symptomatology.

**Methods:** This is a prospective, double-blind two-armed randomized, controlled trial with follow-up at six months to evaluate the acceptability and effectiveness of a case managed strengths approach to proactive integrated HIV care for PHAs compared to usual on demand, self-directed and non integrated service care.

**Results:** Forty-one individuals were eligible and randomized to be part of the study. Twenty-two subjects were randomized to the case management arm and 19 of these completed the 6-month follow-up. Nineteen subjects were randomized to the usual “on demand” care group with three subjects lost to follow-up. The overall completion rate was 85%. The small sample size resulted in the groups being non-equivalent at baseline in demographics, socioeconomics and disease severity.

**Conclusions:** The important findings in this pilot trial are that gender and depressive symptoms were important distinguishing characteristics of PHAs who benefited from either proactive case management or usual self-directed care. Females in the usual group improved the most over the 6-months and generated the most expense. The two management approaches were associated with increased expenditures for depressed.

**Contact Information:** Adriana Carvalhal, Tel: 905-521-2100 x75998, Email: carvalh@mcmaster.ca

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### BARRIERS TO ACCESS TO CANNABIS FOR MEDICAL PURPOSES FOR CANADIANS LIVING WITH HIV/AIDS

Lynne Belle-Isle [1]; Andrew Hathaway [2]
1-Canadian AIDS Society; 2-Centre for Addictions Research of British Columbia

**Plain Language Summary:** Many Canadians living with HIV/AIDS use cannabis (marijuana) to help manage some of their symptoms. Canada has a program to enable people to possess and purchase cannabis legally for their medical needs. However, many people have not obtained legal authorization to possess cannabis and continue to rely on the black market to access their treatment of choice. A survey and focus groups were done to identify barriers to legal access to cannabis for medical purposes. Suggestions are made to address those barriers.

**The Challenge:** North American studies suggest that as many as one-third of people living with HIV/AIDS use cannabis for relief of symptoms. There is clinical evidence to support cannabis’ efficacy to manage symptoms such as appetite stimulation, nausea and vomiting, and pain. Although cannabis remains a controlled substance in Canada, legal access has been granted to people with HIV/AIDS and other serious illnesses under the Marihuana Medical Access Regulations (MMAR) since 2001. Several years into the program, however, few Canadians (about 1800) have obtained MMAR approval, despite the estimated one million Canadians who use it for medical purposes, suggesting that substantial obstacles remain.

**Our Approach:** A survey (n=197) and six focus groups (n=42) were conducted to identify barriers to access to medical cannabis among people living with HIV/AIDS. Survey and focus group participants were recruited using a networking method.

**Key Findings:** Only 26% of current medical cannabis users surveyed had obtained legal authorization to do so. Most (86%) respondents who reported using cannabis for medical purposes continue to rely on illegal sources for their supply. They cited lack of information, product quality concerns, and an onerous, confusing application process among other problems mentioned with the MMAR.

**Impact on Policy and Practice:** Worrying about criminal prosecution to use a treatment of choice, and obtaining a product that is not controlled for safety and quality can have significant negative health effects on people living with HIV/AIDS. Legal options for securing a safe, affordable supply are limited by overly restrictive regulations and other barriers. The findings are discussed in terms of policy suggestions for facilitating access to a legal source of cannabis for medical users.

**Contact Information:** Lynne Belle-Isle, Tel: 613-230-3580 x126, Email: lynneb@cdnaids.ca

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**PHAS AS PEER EDUCATORS, MENTORS, AND ADVOCATES PROGRAM (PEMAP)**

Robert Alexander [1,2]; Francine Small-McHugh [1]; Bridget Marsdin [1]; Mike Kirk [1]; Susan McDonald [1]; Liz Golesic [1]; Orazio Caltagirone [1]
1-The Hamilton AIDS Network; 2-McMaster University

**Plain Language Summary:** The Peer Educator, Mentor and Advocates Program (PEMAP) is a community based, capacity building program that helps volunteers interested in peer education draw upon various resources and diverse experiences in their communities. It is a program rooted in peer support ideology; to promote community awareness, reduce stigma, engage the community and improve the quality of life for all PHAs, and support the GIPA Principle. The PEMAP participants are PHAs and individuals affected by HIV/AIDS.

**The Challenge:** The objectives of The PEMAP Program are to help PHAs cultivate independence, competence, confidence, self-esteem and self-empowerment through our comprehensive training program. The PEMAP Program participants acquire the knowledge and tools necessary to share their experiences with the public and therefore challenge the stigma and discrimination associated with HIV/AIDS by putting a human face on the disease. PEMAP presentations contribute substantially to the community by debunking HIV/AIDS myths, correcting misinformation and disseminating valuable safer sex/prevention education to a diverse range of professionals and community members.

**Our Approach:** PEMAP participants are well –trained in peer counselling and are committed to on-going education and growth, they are an invaluable asset to client support services. PEMAP participants are also well-trained in group facilitation and advocacy skills enabling them to be confident and competent public speakers and advocates thus, enhancing community awareness about HIV/AIDS. A significant component of The PEMAP Program is experiential learning where the participants actively engage in role plays, training and workshops. This offers the participants an opportunity to develop their skills and receive immediate feedback from infected and affected peers.

**Key Findings:** We have had 28 graduates complete the 15 week PEMAP Program. All of the graduates have provided HIV/AIDS educational outreach to the community with medical professionals, social workers, secondary and post secondary students and government employees. The response from the community has been overwhelming and we currently, have a list of agencies interested in receiving The PEMAP Program. There are 10 peer counselors and 6 group facilitators that work with clients through support services on a weekly basis. The peer support that they provide has been an invaluable service to our clients. All of the PEMAP participants have expressed that the program has been beneficial to their lives through the program evaluation. 5 PEMAP participants have made significant life changes, 2 participants have returned to post secondary education and 3 participants have returned to full time employment.

**Impact on Policy and Practice:** The PEMAP Program has enabled PHAs to take greater control of their lives and disease and to develop skills that allow them to apply both practical and professional experiences in providing a wide variety of education services to PHAs and those affected by HIV/AIDS. We are currently working with PEMAP participants in developing a youth expansion to the program. A qualitative evaluation of The PEMAP Program has been conducted and currently we are developing Phase 2 of our evaluation which will focus on quantitative results.

**Contact Information:** Bridget Marsdin, Tel: 905-528-0854, Email: bridgetm@aidsnetwork.ca

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**THE PERCEIVED IMPACT OF TREATMENT INFORMATION FACT SHEETS ON HEALTH-RELATED OUTCOMES ACCORDING TO PEOPLE LIVING WITH HIV/AIDS, HEALTH CARE PROVIDERS AND COMMUNITY CARE PROVIDERS**

Evan Taerk [1]; Timothy Rogers [2]
1-University of Toronto; 2-Canadian AIDS Treatment Information Exchange (CATIE)

**Plain Language Summary:** By providing relevant and reliable treatment information, CATIE attempts to support people living with HIV/AIDS (PHAs) and their caregivers to make informed health-related decisions. Informed decision making can lead to better dialogue with care providers, increased feelings of empowerment, improved adherence and improved care. These factors have been correlated with fewer adverse reactions, delayed disease progression and better health and quality of life. Among the most frequently accessed of CATIE's publications are the fact sheets, which are brief documents, presented in plain language, on a range of treatment-related topics. Despite their widespread use, no systematic assessment of their effectiveness in communicating treatment information has been performed.

**Objective:** To investigate the perceived impact of CATIE's fact sheet series on health-related outcomes (including HIV knowledge, empowerment in decision-making and overall health and quality of life) according to PHAs, health care providers and community care providers.

**Methods:** Retrospective, observational evaluation using a self-administered questionnaire distributed by mail, email and on the Web.

**Results:** 280 surveys were completed with representation from all regions of Canada. The gender breakdown was: 71% male, 27% female, 2% transgendered. 71% of respondents self-identified as living with HIV/AIDS, 17% as healthcare professionals, and 22% as community-based volunteers/workers. The fact sheets series had a positive impact on perceptions of knowledge and empowerment. For example: 99% of respondents agreed the fact sheets were good at addressing their treatment information needs; 97% agreed they felt more empowered to make health decisions as a result of reading the fact sheets; 98% agreed they are better able to assist PHAs as a result of the fact sheets. More than 99% of respondents agreed the fact sheets were helpful for improving the health and quality of life of PHAs, with PHAs tending to agree more strongly than non-PHAs ($p<0.05$). In a qualitative analysis of open-ended questions the following themes emerged: 1) the fact sheets impacted upon health and well being through improved adherence and improved feeling of empowerment to make decisions about treatment; 2) the most useful aspect was that they were up-to-date and easy-to-understand; and 3) the most helpful changes would be to provide more visual information and expand the range of topics.

**Conclusions:** CATIE's fact sheet series are perceived to be effective at increasing health knowledge, supporting health decision making and improving the health and quality of life of PHAs. PHAs rate the impact of this treatment information more highly that others.

**Contact Information:** Tim Rogers, Tel: 416-203-7122, Email: trogers@catie.ca

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### A COMPARISON OF PATIENTS AT AN OUTPATIENT HIV CLINIC

Dawn Elston [1,2]; Lynn Kelleher [1]; Allyson Ion [1,2]; Fiona Smaill [1,2]; Marek Smieja [1,2,3]
1-Special Immunology Services (SIS) Clinic, McMaster University Medical Centre; 2-Department of Pathology and Molecular Medicine, McMaster University; 3-St. Joseph's Healthcare Hamilton

**Plain Language Summary:** The patient profile of the Special Immunology Services (SIS) Clinic, an outpatient HIV clinic, has changed dramatically in the past 10 years. To achieve a better understanding of these changes we compared new patients in 2006 with patients enrolled in the OHTN Cohort Study (OCS). The OCS is a prospective database that has been collecting health information about patients for the past 10 years. The results of this comparison may assist health care providers in providing better quality patient care.

**Objective:** To compare patients admitted to the SIS clinic between January 1, 2006 and December 31, 2006 with patients enrolled in the OCS since 1994.

**Methods:** A retrospective chart review was conducted on 97 new patients. Genotyping results were recorded for new patients only. We compared the results of this chart review with demographic, clinical and laboratory variables in 256 patients enrolled in the OCS in 2006.

**Results:** Of 97 new patients, 37 (38.1%) were women and 60 were men (61.9%). Of 256 OCS participants, 24 (9.4%) were women and 219 were men (85.5%). Of all new patients, 45 (46.4%) list their ethnicity as black; 15.5% white; 1.0% First Nations, and 4.1% South Asian. By comparison, 217 (84.8%) OCS patients are white; 1.2% black, 2.3% First Nations, .8% Asian or Indo-Asian. OCS patients contracted HIV through MSM (62.5%), heterosexual contact (21.1%), IV drug use (14.1%) or blood transfusion (10.2%). Among new patients, 43.3% list heterosexual contact as HIV risk factor; 38.1% are from endemic regions, 16.5% MSM, 11.3% IV drug use and 1.4% blood transfusion. New patients have been HIV positive for 4.69 years on average compared to 14.41 years on average for OCS patients. Rates of opportunistic infections are slightly less in new patients (30.9%) compared to OCS patients (36.7%). CD4 count is higher (mean=326.1, median=295.0) and viral load lower (mean=3.2, median=3.1) in OCS patients than new patients (CD4 mean=304.1, median=250.0; viral load mean=4.1, median=4.4). Clade was determined as a part of genotypic testing. The majority of patients were either Clade B (51.1%) or C (29.8%) A (6.4%); D (2.1%); Mixed (6.4%).

**Conclusions:** Our data demonstrate that the patient profile at the SIS clinic has changed in the past 10 years. Women and racialized groups form a large number of recent referrals to the clinic. Understanding the diverse makeup of our clinic sets the stage for future studies in social inclusion and social determinants of health.

**Contact Information:** Dawn Elston, Tel: 905-521-2100 x73018, Email: elstond@mcmaster.ca

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### POSITIVE SPACES, HEALTHY PLACES: REGIONAL ANALYSES TO PUT RESEARCH INTO ACTION

Ruthann Tucker [1]; Saara Greene [2]; Michael Sobota [3]; Jay Koornstra [4]; LaVerne Monette [5]; Dale Guenter [6]; Steve Byers [7]; James Dunn [8]; Stephen Hwang [8]; Sean B. Rourke [1,8]
1-Ontario HIV Treatment Network; 2-Fife House; 3-AIDS Thunder Bay; 4-Bruce House; 5-Ontario Aboriginal HIV/AIDS Strategy; 6-McMaster University; 7-AIDS Niagara; 8-Centre for Research on Inner City Health, St. Michael's Hospital; University of Toronto

**Plain Language Summary:** This is the first longitudinal community-based research initiative in Canada to examine housing status and stability and its relationship to health outcomes and health related quality of life in the context of HIV and AIDS.

**Our Approach:** A total of 605 face-to-face surveys with people living with HIV and AIDS from across Ontario were collected at baseline (one year follow-up underway) to examine: (a) the housing status of people living with HIV in Ontario; (b) the range of housing and supportive housing options available across Ontario, including those provided by community-based health and social service organizations and other housing agencies; (c) variations in the housing and/or homelessness experiences of people with HIV from specific communities, including aboriginal communities, ethnocultural communities, women, families, sexual minorities, youth and ex-prisoners; and (d) the kind of housing options desired or required by people with HIV that will ensure access to, and utilization of, health care, treatment and social services for optimal health.

**Key Findings:** Housing Opportunities and Supports: (a) Only 15% of sample with housing had support services, which when available, are generally accessible only in GTA, Ottawa and Hamilton; (b) rent geared to income available to only 43% of those sampled; lowest rates in northern regions, Kingston and the GTA; and (c) 42% of sample have significant difficulty meeting monthly housing-related costs and these individuals have significantly lower health-related quality of life relative to those who can make ends meet. Housing Vulnerability and Risk: (a) 21% of sample are at significant financial risk for losing their housing; these rates vary significantly across the province with those in North Bay, Kingston, GTA and Ottawa regions being at the highest risk; (b) 52% of sample face significant anxiety and worry about being forced out of their homes and this is seen at similar rates across province; (c) 35% of sample experienced discrimination when trying to get housing; (d) 1 out of 4 people with HIV do not feel that they belong in their neighbourhood; only 20% feel that their home provides a good place for them to live. Housing Instability: (a) Overall 23% of sample moved in the past year; 57% moved twice or more; (b) moving since HIV diagnosis has dramatic effect on physical health-related quality of life; (c) Moving in past year has significant effect (and stepwise increases with more moves) on both physical and mental health-related quality of life; both effects are likely pronounced because of symptomatic HIV disease of sample. Social Determinants of Health Putting People with HIV More at Risk: (a) 75% of sample report income less than $ 1,500 per month; (b) overall 54% of sample exceeds screening threshold for depression; (c) harmful drug and alcohol use is seen in 27% and 19% of sample; (d) over 20% of sample is dissatisfied with access to health and social services (highest rate seen northern, GTA and Kingston areas); (e) there are significant differences in the rate of persons in study who accessed a family MD in the past 3 months (e.g., 3-4 out of 10 in Thunder Bay and in the Southwest regions did not access an MD).

**Impact on Policy and Practice:** HOUSING SOLUTIONS (1) increase availability of housing opportunities across the full range of housing in the broader housing sector for people with HIV; (2) increase the availability of appropriate housing supports leading to improvements in 'getting and keeping' housing; (3) improve the responsiveness and understanding of non-HIV/AIDS housing service providers; (4) increase collaboration and partnerships to support capacity building; and (5) have government, decision-makers, provincial organizations and researchers undertake more focused housing policy development, advocacy and research initiatives.

**Contact Information:** Ruthann Tucker, Email: ruthann.tucker@shaw.ca

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**WHAT DO PHAS WANT TO KNOW ABOUT ANTIRETROVIRALS?**

Ahmed Bayoumi [1,2,3]; Luisa Frescura [1,3]; Laura Park-Wyllie [3]; Deb Feldman-Stewart [4]
1-Centre for Research on Inner City Health, The Keenan Research Centre in the Li Ka Shing Knowledge Institute of St. Michael's Hospital.; 2-Department of Medicine, University of Toronto; 3-Department of Health Policy, Management and Evaluation, University of Toronto; 4-Cancer Care and Epidemiology, Queen's University

**Plain Language Summary:** Using a series of focus groups and interviews, we determined the key questions that most people living with HIV want answered about the timing and selection of antiretrovirals.

**Objective:** Both people living with HIV/AIDS (PHAs) and their clinicians must consider multiple risks and benefits, some unknown, when deciding about the timing and selection of antiretroviral therapy. Constraints on clinicians' time and abilities may limit the utility of the clinical encounter for facilitating such difficult decisions. We determined the information needs of PHAs and clinicians for decision making about antiretrovirals.

**Methods:** We conducted focus groups and interviews using a semi-structured guide. Each interview was coded by two study investigators to identify questions that PHAs might want answered regarding antiretrovirals. Next, we conducted 44 interviews with PHAs recruited through advertisements, AIDS service organizations, and clinics. Each respondent rated potential questions on a 4-point scale (Essential, Desired, No Opinion, or Not Important). We calculated how frequently participants agreed with each other about the importance of a question, weighting responses so that disagreement between "Essential" and "Desired" categories was discounted. We identified the most important questions by calculating how frequently participants agreed that a question was "Essential", allowing us to identify the questions about which there was most consensus regarding their importance.

**Results:** We conducted 6 key informant interviews (3 physicians, 2 pharmacists, 1 nurse) and 2 focus groups with PHAs, one each for men and women. We generated a list of 147 potential items applicable to all individuals (reported here), 2 items relevant to refugee claimants and 6 items relevant to women. Of 44 interviews, 2 were not usable. The average age of participants was 46.5 years (SD 8.4), 92% were men, 58% white, 8% black. The most recent median CD4 count was 450 cells/mm3, 61% had an undetectable viral load, and 71% were using antiretrovirals. The average weighted agreement across all items was 63% (range 33% to 91%). The most important items questions about CD4 counts and the nature of HIV, short- and long-term adverse events, drug interactions, durability of antiretroviral activity, cost, approach to missed antiretroviral doses, and specific adverse events (including neuropathy, liver damage, body shape changes, and mood changes).

**Conclusions:** We have identified the key information needs of people living with HIV. We will use these questions to inform the development of a decision aid to assist PHAs with difficult decisions regarding antiretrovirals.

**Contact Information:** Ahmed Bayoumi, Tel: 416-864-5728, Email: ahmed.bayoumi@utoronto.ca

## Global Issues

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**BRAZILIAN AND CANADIAN AIDS/NGOS AND THE FIGHT AGAINST SOCIAL DISCRIMINATION AND STIGMA**

Carlos Roberto Castro-Silva [1]; W.E. (Ted) Hewitt [2]
1-Faculty of Psychology, Universidade Cruzeiro do Sul ; 2-Department of Sociology, University of Western Ontario

**Plain Language Summary:** People living with HIV/AIDS (PHAs) have faced many difficulties in the course of their lives. These people suffer discrimination in different contexts such as familiar, collective and professional. Currently, AIDS-related non-governmental organizations (AIDS-NGOs) are becoming increasingly important because, besides providing those people with traditional social aid, they also offer an environment which may allow PHAs not only to express themselves openly, but also to share their own experiences with HIV/AIDS.

**Objective:** Through this study, we discuss AIDS/NGO as a place for combating the effects of social discrimination and stigma suffered by PHA. Specifically, we examine a variety of psychosocial mechanisms operating through these groups (PHAs who are engaged with AIDS-NGOs) which contribute to the reduction of the stigma and social discrimination experienced by PHA.

**Methods:** We analyze historical documents, in-depth interviews, and questionnaires answered by community members from two AIDS-NGOs: one located in London, Ontario (NGO-Ca) and other located in Sao Paulo city and its surroundings, in Brazil (NGO-Br).

**Results:** We discourse on some pathways for political participation which are relevant to both communities and may contribute to the diminution of stigma and discrimination related to HIV/AIDS: Compassion and altruism as a bridge to political participation, Effects on activism, and Fostering based on solidarity and co-responsibility.

**Conclusions:** To participants of NGO-Br the HIV/AIDS impact is stronger because they feel abandoned and feel no respect as individuals and citizens. In this way, the NGO-Br setting represents an important place to access their rights. Furthermore, there they may collectively build these rights. Somewhat, differently, participants of NGO-Ca see the institution as a place where they can access their citizenship status. In addition, we observed that the process of institutional democratization is a relevant aspect to strengthening personal development and citizenship. In NGO-Br relationship of power between participants must be reviewed. In NGO-Ca, incentives for political activism must be reviewed.
The study suggests the strengthening of practices that promote individuals to the status of citizenship. These practices can start right at the reception of PHAs by the NGO through projects designated to strengthen his/her self-esteem. Understanding and welcoming different ways of political participation means valuing a psychosocial perspective, that is, to notice a process of subjective and psychological changes in an inevitable interaction with the social-historical and cultural context that leads to psychosocial emancipation. This emancipation should run in parallel with the strengthening of these individuals and their full citizenship.

**Contact Information:** Carlos Roberto Castro-Silva, Tel: 55-11-3667- 0068, Email: carobert@usp.br

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**SLOW PROGRESSION OF PEDIATRIC HIV DISEASES: SELECTIVE ADAPTATION OR A CHANCE PHENOMENON**

Misaki Wayengera [1]
1-Makerere University Faculty of Medicine-Uganda and Restrizymes Corporation Canada

**Plain Language Summary:** Disease progression in Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) is affected by several factors both external and internal to the human hosts. In the European Caucasian populations, the Chemokine-cell receptor variant CCR5 "Delta 32" is a genetic determinant of HIV disease progression that is believed to have been selected for in the general population by exposure to antigens closely interlinked to HIV like Yersinia pestis or small pox virus. Among African populations, it is possible that this selection will be induced by HIV over time.

**Objective:** To present two cases of mother to child transmitted HIV highlighting the possible increasing prevalence of slow disease progression.

**Methods:** Clinical case reports of slow progression of pediatric HIV.

**Results:** Both patients were female, had lost one parent >10yrs prior but had the other surviving parent exhibiting slow HIV disease progression. We question the possible inheritance of the genetic factors associated with slow disease progression in a recessive X-linked Mendellian pattern and the role of the high prevalence of HIV within the sub-Saharan setting as the selective pressure favoring the establishment of the currently known immunologic and genetic factors influencing HIV diseases progression.

**Conclusions:** A more in-depth immunologic and genetic approach is called for to further examine the baseline prevalence and possibility of adaptive selection for immunogenetic protectors of HIV disease progression within the sub-Saharan setting.

**Contact Information:** Misaki Wayengera, Tel: 647-409-1979, Email: wmisaki@yahoo.com

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### INVESTIGATING THE BIRTH OF AN HIV-1 EPIDEMIC; MOLECULAR ANALYSIS OF THE SARGODHA, PAKISTAN IDU OUTBREAK

Richard Pilon [1]; Rana Muzzaffar [2]; Muhammad Agha Babar [3]; Salma Batool [2]; Dominic Vallée [1]; Naeem Hasan Saleem [4]; Faran Emmanuel [4]; Paul Sandstrom [1]
1-National HIV & Retrovirology Laboratories, Public Health Agency of Canada; 2-Sindh Institute of Urology and Transplantation (SIUT), Pakistan; 3-Armed Forces Institute of Pathology (AFIP), Rawalpindi, Pakistan; 4-HIV/AIDS Surveillance Pakistan (HASP), Pakistan

**Plain Language Summary:** There is tremendous diversity in the HIV epidemic owing to the virus' rapid rate of evolution. This evolution occurs at a constant rate; therefore, when transmissions are from a common source (A to B, C & D or A to B to C to D, or any combination in between) over a short timeframe, there are few differences between the transmitted viruses. Using phylogenetic methods, we are able to measure these differences and evaluate relationships between infections, essentially generating a "family tree". This was the approach taken for a cluster of infections detected in early 2007 among injection drug users (IDU) in Sargodha, Pakistan. Within this high risk population, our study found that 95% of the infections originated from a common source in a relatively short timeframe, which suggests an HIV outbreak in this high-risk and previously low-prevalence population.

**Objective:** To evaluate the molecular characteristics of an apparent HIV outbreak among IDU in Sargodha, Pakistan in early 2007.

**Methods:** Comparative phylogenetic analyses were performed on HIV pol (protease and RT) and env gp41 sequences generated from dried blood spots (DBS) collected from 400 IDU as part of the Canada-Pakistan HIV/AIDS Surveillance Project. We used the Neighbor-Joining method with Kimura 2-Parameter model and bootstrap re-sampling as implemented in MEGA3.1. Within cluster distances were compared to those from Canadian transmission clusters.

**Results:** The prevalence of HIV among Sargodha individuals at high risk of infection was 0%, 0.5% and 1.0% among female (n=400), hijra (n=200) and male (n=200) sex workers, respectively, and 51.5% for IDU (n=400). Sequencing attempted on the 200 available HIV positive IDU DBS generated 151 sequences (75.5%). Phylogenetic analysis revealed these to be subtype A1 (n=143) and CRF02_AG (n=8). Further analysis revealed clustering of the sequences into two distinct infection groups: 142 within subtype A1 and 7 within CRF02_AG. The mean distance between clustered Sargodha pol sequences was 0.41% and 1.45%, respectively, for each cluster, and 0.36% between clustered Polaris sequences. Similarly, analysis of env gp41 revealed distances of 0.80% and 0.72% for the A1 and AG clusters, respectively, and 0.34% for sequences from a well characterized transmission cluster.

**Conclusions:** Based on the findings of this analysis, the majority (95%) of specimens formed a distinct cluster of highly similar sequences, suggestive of a recent, common source of infection, and a true outbreak among the Sargodha IDU population. Until recently, Pakistan has been a high risk, low prevalence country. The time is now for aggressive prevention.

**Contact Information:** Richard Pilon, Tel: 613-954-1278, Email: richard_pilon@phac-aspc.gc.ca

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### HIV/AIDS CONTROL IN PRISON SYSTEMS OF THE FORMER SOVIET UNION: CURRENT STATUS AND FUTURE OPTIONS

Saba Khan [1,2,4]; Peggy Millson [1,2,3]; Catherine McLaughlin [1,2]; Prabhat Jha [1,2,4]
1-Centre for Global Health Research; 2-St. Michael's Hospital; 3-HIV Social, Behavioural and Epidemiological Studies Unit, University of Toronto; 4-Public Health Sciences, University of Toronto

**Plain Language Summary:** HIV/AIDS is a major health concern in prison systems around the world. This reflects the elevated prevalence of infection in persons entering prison, as well as sexual and drug-related risk behaviors occurring during incarceration. In countries of the Former Soviet Union (FSU), the prison HIV epidemic is primarily driven by injecting drug use. However, there is little information documenting HIV/AIDS levels and intervention strategies in FSU prisons.

**Objective:** To determine the most effective and widely used HIV/AIDS prevention and treatment strategies currently implemented in prison systems globally and to use this information as evidence towards recommendations for FSU countries.

**Methods:** A systematic literature review was undertaken in order to examine the published literature on HIV/AIDS interventions in prison systems worldwide and the current status of FSU prison interventions.

**Results:** Interventions that have proven effective in combating HIV/AIDS in prisons include needle and syringe programs, condom distribution, opioid substitution therapy, antiretroviral therapy, HIV/AIDS education, and voluntary counseling and testing. FSU countries are at differing stages of acceptance and implementation of HIV/AIDS programs in prisons. Data on HIV/AIDS interventions in prisons in the FSU are minimal. Kyrgyzstan is provided as a case study of a more advanced model of FSU prison interventions.

**Conclusions:** HIV/AIDS prevention and treatment programs must be initiated or scaled up in all FSU prison systems in order to fully control the growing epidemic. Governments must recognize that prisons are a key setting for implementing a comprehensive model of HIV/AIDS interventions and should demonstrate their commitment to prison health by providing funds and amending current policies.

**Contact Information:** Katie McLaughlin, Tel: 416-864-6060 x3321, Email: mclaughlinc@smh.toronto.on.ca

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### RISK PERCEPTION AND SEXUAL BEHAVIOURAL CHANGE AMONG YOUTH IN CAPE TOWN, SOUTH AFRICA

Eric Y. Tenkorang [1]
1-Department of Sociology, University of Western Ontario

**Plain Language Summary:** The 'Health Belief Model' (HBM) identifies perception of HIV/AIDS risks and knowledge about AIDS transmission as major correlates of sexual behavioural change. Risk perception is for instance considered an essential, and indeed the first step towards change from risk-taking to safer sex.

**The Challenge:** This notwithstanding, results from studies that attempt to establish an association between risk perception and sexual behavioural change are mixed. In addition to this, very few studies have attempted to establish a causal link between risk perception and behavioural change.

**Our Approach:** This study examined the relationship between perception of HIV/AIDS risks and sexual behavioural change among youth aged 14-22 in Cape Town, South Africa using data from the Cape Area Panel Survey (CAPS). Sexual behavioural change is measured in terms of the timing of sexual intercourse, use of condoms at both first and last sexual intercourse and multiple sexual partnerships.

**Key Findings:** Results indicate that youth with high perception of contracting HIV/AIDS experience their sexual debut later than those with no or low perceptions of catching HIV/AIDS after controlling for other theoretically relevant variables. Similarly, youth with high risk perceptions were more likely to have used condoms at both first and last sexual intercourse, and less likely to have had multiple sexual partners compared to those with no or low risk perception. Knowledge about AIDS was also a significant predictor of sexual behavioural change, especially among young South African females. High knowledge about HIV/AIDS translated into safe sex behaviours, while low knowledge about the disease encouraged risky sexual behaviours.

**Impact on Policy and Practice:** From a policy standpoint, we recommend that policy makers work on changing the risk perception of youth in South Africa as a way of achieving the expected behavioural change needed for reversing the trend in prevalence rates. Policy makers must continue to support the dissemination of HIV/AIDS information given its impact on risk perception and consequently, sexual behavioural change.

**Contact Information:** Eric Y. Tenkorang, Tel: 519-661-2111 x85150, Email: ytenko@yahoo.com

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### A GLOBAL SURVEY OF HIV/AIDS AND PREDICTIONS AS TO FURTHER AFFECTS ON THE INTERNATIONAL COMMUNITY

Leon Sanders [1]; Brahmananda Reddy [1]
1-Grambling State University

**Plain Language Summary:** HIV/AIDS continues to grow in infection rates and prevalence across the world. Many different factors are studied and surveillance information is compiled, however a complete picture of the HIV/AIDS epidemic in each country does not exist. This is due to a lack of information in many researched areas such as the reported HIV/AIDS cases within a country or the amount of government spending disbursed for HIV/AIDS.

**Objective:** This study attempts to work around some of the areas that lack information and to compile a more complete picture of the HIV/AIDS epidemic than currently exists in the scientific literature.

**Methods:** We examined the nature of HIV, its modes of transmission, differing subtypes, risk factors, difficulty in eradication, diagnosis, and then its impact on national economies. We then assessed the economies, education, government spending, and HIV prevalence for approximately 35 countries. Related work in various countries and regions was also studied to review other possible factors that have been studied in HIV survey research.

**Results:** The study concludes that the number of socioeconomic, political, behavioral, and economic factors involved in the HIV/AIDS epidemic vary from country to country. The study has shown that the most affected age group for men in the world as well as independent countries is 25 to 40 and for women is 20 to 40. The study identified that poverty, education, and government spending comprised small part of the factors that characterize the HIV/AIDS epidemic. Also, the reported HIV/AIDS case data is incomplete from 2003-2006 in many countries, skewing the interpretation of data from 1985 to 2006.

**Conclusions:** HIV/AIDS epidemics differ from country to country in their causes, sub-population infection rates, as well as the prevention methods necessary to deal with each respective HIV epidemic. The related work compiled in this study along with its findings demonstrates that a diverse range of factors apply in each nation, more than just education, poverty, and government spending. Thus a comprehensive HIV/AIDS prevention/treatment plan will take into account social, behavioral, economic, and educational areas. HIV/AIDS infects the most productive age group (20 to 40) of a population and is thus a threat to the socioeconomic growth and survival of all nations. In some countries different subpopulations must be targeted such as IDUs, and rape victims. Unless we target these sub-populations and age groups, it will not be possible to prevent the HIV/AIDS epidemic from further escalating.

**Contact Information:** Leon Sanders, Tel: 502-229-6609, Email: lss8@pitt.edu

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### HIV AND AIDS POLICY DEVELOPMENT IN A UNIVERSITY COMMUNITY

Anitha Menon [1,4]; Sarah Jane Taleski [2,5]; Mulenga Musepa [3,4]
1-Department of Psychology, University of Zambia, Lusaka, Zambia; 2-Centre for International Health, University of Toronto; 3-Public Affairs, University of Zambia, Lusaka, Zambia; 4-University HIV/AIDS Committee, University of Zambia, Lusaka, Zambia; 5-HIV Response Office, University of Zambia, Lusaka, Zambia

**Plain Language Summary:** The University of Zambia (UNZA) is responsible for building the capacity of trained personnel within the country. As a university, UNZA is by definition an educational institution and the significance of its role in HIV and AIDS prevention, care and treatment may not be immediately apparent. However, HIV and AIDS affects all areas of UNZA's core business- teaching and learning, research and community engagement- and the entire university community. There is need to assign funding to not only prevention, care and treatment but also to account for the costs associated with staff and student attrition. HIV is interconnected with both the function and role of UNZA on multiple levels making the necessity of adopting an HIV/AIDS policy evident.

**The Challenge:** The dynamic and unique institutional structure of a university requires considerations beyond that required for other institutions. UNZA is an education institution dedicated to its students, a workplace accountable to its staff and a community leader. The utility of broad-based national and labour policies in the multi-dimensional nature of a university is limited. Institutional policies offer benefits beyond that which can be gained through the application of national, or ministry policies. Given this and the need to design a policy meeting the specific needs of the UNZA community an interactive process was employed in the development of the UNZA HIV and AIDS policy.

**Our Approach:** Regional university policies were reviewed to develop the draft working policy document which was adapted to the UNZA context and circulated to all the key stakeholders: students, academic staff and non-academic staff. Responses from the stakeholders were consolidated and recirculated before a consensus document was formed.

**Key Findings:** The following key objectives to be addressed by the policy were identified; 1) Providing guidelines for HIV and AIDS related decisions and activities; 2) Providing an environment free from discrimination; 3) Providing information, education, counseling and supportive care services to enhance wellbeing of those infected and affected by HIV and AIDS. Although many issues raised were similar to those seen in policies found at regional tertiary education institutions, the issue of sexual harassment was a new dimension which emerged.

**Impact on Policy and Practice:** The policy was formulated to establish guidelines for decision-making, coordination and action as well as provide a safe learning and working environment for students, staff and their dependants. Utilizing an interactive process ensured that the policy was specific to the needs of UNZA and created a shared ownership of the policy among the UNZA community.

**Contact Information:** Sarah Taleski, Tel: 416-451-2610, Email: sarahtaleski@gmail.com

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### HIV AND TB KNOWLEDGE AMONG HEALTHCARE PROFESSIONALS AND STUDENTS IN GEORGETOWN, GUYANA

Louise Balfour [1]; Giorgio Tasca [1]; Kimberly Corace [1]; Wallis Best Plummer [2]; Curtis Lafleur [2]; Jadunauth Ragunauth [3]; Paul MacPherson [1]; Karamchand Ramotar [1]; D. William Cameron [1]
1-The Ottawa Hospital-General Campus; 2-Public Health Strengthening in Guyana Project (PHSGP), Georgetown, Guyana; 3-Genito-Urinary-Medical (GUM) Clinic, Georgetown, Guyana

**Plain Language Summary:** The present study examines the impact of targeted training on HIV and TB knowledge among healthcare providers and students in Guyana. Results indicated that healthcare professionals and students who received targeted HIV and TB training courses had higher HIV and TB knowledge scores. Gaps were identified in both HIV and TB knowledge regarding complex treatment issues (e.g., adherence to medications). In addition, healthcare providers and students with higher levels of HIV stigma had lower levels of HIV knowledge.

**Objective:** The prevalence of HIV-TB co-infection is very high in developing countries such as Guyana. From a healthcare infrastructure building perspective, examining healthcare providers' knowledge of HIV and TB and the impact of educational initiatives aimed at reducing gaps in knowledge is important. Our goal was to examine HIV and TB knowledge and the impact of targeted training among healthcare providers and health science students in Guyana.

**Methods:** Students and healthcare workers were recruited from: (1) a seminar series at the University of Guyana, and (2) a continuing education workshop for pharmacists in Guyana. A total of 83 health science students (e.g., medical students) and 55 healthcare professionals (e.g., pharmacists) completed questionnaires on HIV and TB knowledge and stigma. Participants indicated if they had previously attended any HIV or TB structured training sessions, such as those developed and provided through a partnership initiative between the CIDA funded Public Health Strengthening in Guyana Project (PHSGP) and the Ministry of Health in Guyana.

**Results:** Overall, healthcare professionals had significantly higher HIV knowledge scores than health science students. Both health professionals and students who had received targeted HIV training had significantly higher HIV knowledge scores than those without targeted training ($p<.05$). Similarly, health professionals and students who received targeted TB training had significantly higher TB knowledge than those without targeted training ($p<.05$). There were significant gaps in both HIV and TB knowledge regarding complex treatment issues (e.g., optimal adherence, drug resistance). In addition, HIV stigma was related to poorer levels of HIV knowledge.

**Conclusions:** Targeted HIV and TB educational seminars were associated with higher knowledge scores. In addition, HIV stigma was related to poorer levels of HIV knowledge. These results highlight the importance of developing and providing ongoing targeted HIV and TB educational training.

**Contact Information:** Kimberly Corace, Tel: 613-737-8866, Email: kcorace@ottawahospital.on.ca

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### INTRODUCING A PATIENT MENTORSHIP PROGRAM AT ZOMBA CENTRAL HOSPITAL, MALAWI

Marion Kambanji [1]; Barry Burciul [1]; Matthew Chan [2]; Dignitas International Research Group
1-Dignitas International Research Group; 2-Faculty of Health Sciences, McMaster University

**Plain Language Summary:** Uptake of, and adherence to ART can be inhibited by stigma and a lack of support structures for patients beginning therapy. These problems are compounded by a dearth of health care professionals and clinic support staff, which forces staff to divide their time between patient-support and their other assigned activities.

**Objective:** To involve several "Expert Patients" (EPs) as volunteers in providing support and orientation for new and prospective ART patients, with a view to increasing treatment uptake, enhancing patient morale, and easing the workload on clinic staff.

**Methods:** During refresher training for patients on ART for six months, 13 patients volunteered as EPs. EPs serve as positive role models of successful ART, counsel patients on ARVs and positive living strategies, familiarize them with staging and ART, and guide them through the hospital. They also perform clinic support functions including translating for non-Chichewa clinic staff, assisting nurses during patient consultations, weighing patients, booking patients for counselling sessions, filing records, and cleaning. One EP has been trained to help nurses prepare IV fluids. EPs are present from 7am to 5pm.

**Results:** At six months, 7 of the original 13 EPs remain. Those who left did so because of a lack of reliable transportation. The remaining number of EPs is sufficient for the current patient load. EPs have provided nurses with more time to assess patients, increased the number of patients that a nurse can see in a given time, and provided continuity of clerical services during clerk's absences. EPs are now well accepted by staff and patients.

**Conclusions:** EPs have provided valuable supplementary support at the ZCH ART clinic. Moving forward, we plan to evaluate and further train EPs, and to explore the feasibility of introducing the program in ART sites at Health Centres.

**Contact Information:** Barry Burciul, Tel: 416-260-3100, Email: b.burciul@dignitasinternational.org

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### COLLECTION AND REPORTING OF PATIENT ART ADHERENCE DATA IN ZOMBA, MALAWI

Sumeet Sodhi [1,2]; Alexis Palmer [3]; Dignitas International Research Group
1-Dignitas International Research Group; 2-Department of Family and Community Medicine, Toronto Western Hospital; 3-Faculty of Health Sciences, Simon Fraser University

**Plain Language Summary:** In HAART therapy, high levels of adherence are essential for complete and long-term viral suppression, and the avoidance of drug resistance. Common methods of adherence measurement and reporting include pill counts, electronic monitoring, pharmacy record reviews, and self-reporting. There is widespread concern regarding the quality of adherence data.

**Objective:** This study examines reliability issues pertaining to the quality of data gathered from pill counts and those relating to the transcription and flow of this and other adherence data.

**Methods:** We observed the existing processes of data collection and flow at the main ARV clinic and other Dignitas-supported ART sites, conducted key-informant interviews, and analyzed the findings in light of the existing literature regarding adherence monitoring and reporting.

**Results:** There were incomplete patient files with inconsistencies in recordings and terms used. There is a need for greater training and education among the health clinic staff. A major problem identified was the transfer of data from decentralized sites to the main site at Tisungane clinic. The strain on human resources in the region is affecting the staff motivation and the quality of their work. Time restraints results in less patient time and increased opportunities for human error in reporting adherence. To remedy this human resource problem, Expert Patients are paying an invaluable role in the clinic setting. The data entry clerk in charge of entering the adherence data is overburdened with her workload.

**Conclusions:** There is a need for an advancement of technology in the area of data collection and reporting. Point-of-care, real-time reporting is now starting to be offered in Malawi. A computer system that would standardize and record information as it is being collected from the patient and then be sent directly to a main database would be an ideal solution. All of the paperwork moving from site to site encourages loss and human error and uses up valuable person time in an already overstretched health care system. The current Dignitas model of decentralization is a perfect opportunity to test the merits of a point-of-care technology network.

**Contact Information:** Sumeet Sodhi, Tel: 416-260-3100 x109, Email: s.sodhi@dignitasinternational.org

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**INTERVENTIONS, HIGH RISK BEHAVIORS AND ITS INTERACTION ON HIV EPIDEMIC: MULTILEVEL MODELING ON HIV IN INDIA**

Li Chen [1]; Prabhat Jha [1]; Catherine McLaughlin [1]; Wilson Suraweera [1]; Celia Zhao [1]; Nico Nagelkerke [1]
1-Centre for Global Health Research, St. Michael's Hospital, University of Toronto

**Plain Language Summary:** A multilevel model was hired to quantitively evaluate the activities of HIV prevention for high risk groups (1998-2004) on HIV infections among 115 districts in Southern India, assess the variability of HIV among districts, and investigate the relationship of risk behaviors on high risk men and other district-level factors with individual HIV infection.

**Objective:** HIV in southern India has drawn attention since 1998, and many intervention programs have been conducted on high risk people, especially for female commercial sex workers (FSW), by government, and non-government organizations. The activities include distributing condoms, treating sexual transmitted infections (STI), and education programs. Although there showed a slight decrease trend in HIV prevalence for people at younger age (15-24), HIV is still very high in the south, more than 1% for general population at 2000-05. The extent of the effect of interventions on HIV epidemic needs to be measured. On the other hand, the main driving factors, ecological and individual, for HIV epidemic are still not clear. The objective of this study is to quantitively establish the impact of HIV intervention programs on HIV, and study the risk factors for HIV infection at both individual and district level.

**Methods:** A two-layer hierarchical logistic model with random coefficients was presented. HIV status for 400 females at antenatal clinic in each district (2005) was modeled step by step according to individual factors and district variables. District level factors included intervention details (such as year, type, size, activities), baseline HIV prevalence at 2000-04, high risk behaviors and STIs on males from sexual transmitted clinics, STI for general female and male, and some other factors associated with HIV, such as male circumcision and marital status.

**Results:** The heterogeneity of HIV infection among districts is significant. The peak change of condom distribution on intervention showed a positive relationship with HIV infection (OR=2.0), and the STI treatment for FSW had a negative effect (OR=0.34). STI and HIV at STI clinics strong positively related to HIV infection and showed the interaction with STI treatment. Age, education, syphilis related to HIV as well.

**Conclusions:** Individual risk factors and ecological variables, especially for risk behaviors for high risk man, explained the main part of the variability of HIV in southern India. It suggested that more prevention programs should focus on male high risk groups, in addition to FSWs.

**Contact Information:** Li Chen, Tel: 416-864-6060 x3315, Email: chenli@smh.toronto.on.ca

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**HIV TREATMENT IN DAR-ES-SALAM, TANZANIA: A RETROSPECTIVE CHART REVIEW**

Astha Ramaiya [1,2]; Kaushik Ramaiya [1]; Marek Smieja [2,3]
1-Shree Hindu Mandal HIV clinic, Dar-Es-Salaam, Tanzania; 2-St. Joseph's Hospital, St. Joseph's Hospital; 3-McMaster University

**Plain Language Summary:** This chart review examined the outcomes of 560 patients attending the Shree Hindu Mandal HIV clinic in Dar-Es-Salaam, Tanzania over 10 years (1997 – 2007). Of 286 people with information on ARVs, 182 were started on ARVs and 104 were not. ARV use in this resource-poor setting was associated with high compliance and low mortality, although adverse events were a common cause of ARV regimen change. Costs remain a significant barrier to accessing doctors, laboratory resources, and ARVs.

**Objective:** To look at the effectiveness and tolerability of ARV treatment in adult patients in Tanzania, a sub-Saharan African resource-poor endemic country, over 10 years.

**Methods:** A total of 560 subjects were recruited based on the medical files and case notes. A database was created in Epi Info that recorded the identification and background of the patient, the clinical characteristics, past medical and family history and the physical examination. Laboratory tests were abstracted. In addition, patients were asked to return for follow up to assess the effect of treatment.

**Results:** Of 560 subjects with a clinical suspicion of having HIV infection, presenting to the Shree Hindu Mandal HIV clinic in Dar-Es-Salam, Tanzania, there were an equal number of males and females (n=273) and 14 did not respond. Age ranged from 3 to 76 years, with a mean (standard deviation) of 41.3 (10.6) years. HIV testing was available in 442 subjects, of whom 30 (6.8%) were negative and 412 (93.2%) were positive. Hence, the clinical diagnosis of HIV was highly specific and usually confirmed by laboratory testing. Of the 560 subjects who had their first visit recorded, 286 people had follow-up information on ARV use. Of these, 182 (63.6%) were on ARVs and 104 (36.4%) were not. Between 1997 and 2007, a total of 5197 follow up visits from the 286 people were recorded (mean of 18 visits per person). At each visit, treatment outcomes were assessed. During 197 visits, a change in medication was recorded (mean of 1.1 per person), while during 5000 visits medications were not changed. The reasons for medication change were side effects (50%), poor response to the medication (29.3%) and cost (20.7%). Recorded outcomes were: 92.4% had good compliance, followed by 7.1% reduced compliance, eight patients (4.4%) were lost to follow-up or transferred, and six patients (3.3%) died.

**Conclusions:** Our data has limitations inherent to retrospective clinical research. Estimates may be skewed by multiple visits over time by patients who have done well, and by limited follow-up in more recent patients. Nevertheless, our data show that ARV treatment is feasible with good outcomes and compliance in a resource poor setting. However, 20% of subjects changed drugs due to cost, and likely many more were unable to afford to see a doctor, to pay for laboratory testing (CD4 counts) or to purchase ARVs. Tanzania is a one of the poorest countries in the world, and world-wide support is required to adequately resource treatment programs in sub-Saharan Africa.

**Contact Information:** Astha Ramaiya, Tel: 905-522-1155, Email: aramaiya@stjoes.ca

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### ADMINISTRATION OF THE SÃO PAULO STATE STD/AIDS PROGRAM (BRAZIL): ANALYSIS OF THE ACTIONS DECENTRALIZATION PROCESS FROM 1994 TO 2003

Renato Barboza [1]; Ligia Rivero Pupo [1]
1-Health Institute - State Health Secretary of São Paulo, Brazil

**Plain Language Summary:** The convention loans for AIDS established by the Health Ministry and the World Bank from 1994 to 2002 were fundamental to consolidate the programmatic actions and to control the AIDS epidemic in the country. Despite progress in areas such as prevention and assistance, administration of the programs presented a low degree of institutionalization in the National Health System related to difficulties for planning, monitoring and evaluating the programmatic actions. This situation increases the social and institutional vulnerability for STD/AIDS in São Paulo State.

**Objective:** This qualitative study analyzed the implementation of the São Paulo State STD/AIDS Program from 1994 to 2003 concerning decentralization and administration of the actions in its administrative, technical and policy dimensions.

**Methods:** For this qualitative study four Municipal Health Departments were intentionally selected. Interviews with managers from the three governmental levels were also carried out. Administrative papers about the agreement with the World Bank and the incentive policy of funding transference established in 2003 in the Health Department of the State and the Municipal Health Departments were analyzed.

**Results:** Findings showed that in the State 37 municipal districts were covenanted in the loan agreement period and 101 new municipal districts were included with the establishment of the policy of funding transference which enlarged the decentralization of the programmatic actions. This process has presented different degrees and distinct operative forms, according the administrative level investigated. The main identified difficulties to implement the action plan agreed with the National Health System are related to the lack of professionals prepared for administering, monitoring and evaluating the actions.

**Conclusions:** The incentive policy of funding transference established by the Ministry of Health has intensified the decentralization process, transferring the decision power to the State and municipal districts, improving administration of STD/AIDS public policies. However, evaluation and monitoring of the actions need to be qualified given priority to the new municipal districts included in the incentive policy of funding transference. This decision is quite important to reduce the institutional and social vulnerability in São Paulo State STD/AIDS Program and strengthen prevention and assistance activities.

**Contact Information:** Renato Barboza, Tel: 5511-31515346, Email: renato@isaude.sp.gov.br

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### PREVALENCE AND RISK FACTORS FOR HIV OF MALE STI CLINIC ATTENDEES IN INDIA: HIV SENTINEL SURVEILLANCE, 2005

N. Driver [1]; S. Mishra [1]; P. Jha [1]
1-Centre for Global Health Research, St. Michael's Hospital, University of Toronto

**Plain Language Summary:** Sexually transmitted infections (STIs) facilitate transmission and infectiousness of the Human Immunodeficiency Virus (HIV) through direct, biological mechanisms. Because patients seeking treatment for STIs are more likely to engage in high-risk sex, this bridge population has been used as sentinels in HIV surveillance. In India, patients who attend STI clinics are managed syndromically and in addition to HIV, are tested for syphilis and other STIs using unlinked, anonymous testing. This surveillance data has been primarily used to monitor HIV trends; prevalence of STI signs such as, genital ulcer and discharge, and the interrelationships between HIV and signs have not been examined.

**Objective:** To describe the HIV, genital ulcer (GU), and urethral discharge (UD) prevalence and examine the risk factors for HIV of male STI clinic attendees in 'south' India.

**Methods:** Data was obtained from the Government of India's National AIDS Control Organization for the year 2005. Only males 15-49 years were considered in this analysis. 'South' India was defined by the states of Andhra Pradesh, Karnataka, Maharashtra, and Tamil Nadu. Crude prevalences were calculated for all positive cases of HIV, GU, and UD. HIV prevalence was also stratified by state and 5-year age categories. Univariate logistic regression was used to examine the relationship between HIV and demographic variables, STI signs, and Venereal Disease Research Laboratory (VDRL) results.

**Results:** In 2005, the 5328 males 15-49 years old were tested for HIV. The HIV prevalence of 'south' India was 17.5% (95% CI: 16.5-8.6%). The range of HIV prevalence among the four states was 12.1% - 21.4%. Approximately 50% (95% CI: 49.1-51.8%) of STI attendees had GU while, UD was prevalent in 35.6% (95% CI: 33.3-35.9%) of the population. Males 35-39 years old had the highest HIV prevalence (22.8%, 95% CI: 19.9-25.7%). Being illiterate, having a positive VDRL result, and presenting with a GU increased the odds of being HIV positive. Only literacy and the VDRL result showed a statistically significant association. The odds of HIV positivity was significantly lower among males with UD compared to those without.

**Conclusions:** HIV and STIs are common in STI sentinel population. Further multivariate work is required to better estimate the magnitude of HIV risk factors. An inverse association between HIV and urethral discharge is contrary to most reports in the literature and raises the need for hypothesis generation. A better understanding of the relationships between HIV and STIs might be helpful in identifying a surrogate STI marker for HIV.

**Contact Information:** Natasha Driver, Tel: 416-864-6042 x3303, Email: drivern@smh.toronto.on.ca