

BC Liberals commit to HIV/AIDS pilot project

Premier Gordon Campbell announced a commitment to a pilot project that will expand access to HIV and AIDS drugs to the street-involved population in downtown Prince George and Vancouver's Downtown Eastside. The program will decrease AIDS-related suffering and further prevent the spread of HIV disease.

"People living on the streets and other 'hard to reach' populations are much less likely to access appropriate care and support or to have a family doctor, and are more likely to have undiagnosed and untreated HIV/AIDS," said Premier Campbell.

"Through the excellent work of Dr. Julio Montaner and the BC Centre for Excellence in HIV/AIDS, a pilot project is being proposed to connect with people on an individual basis and get them a chance to access the services they need."

Both downtown Prince George and the Downtown Eastside of Vancouver are areas which have been profoundly affected by HIV/AIDS. The pilot will involve integration by health system partners from public health and non-governmental community-based organizations, to low-threshold interdisciplinary primary care clinics and private practice physicians. While the proposal will facilitate access to HIV testing and care, engagement will be strictly voluntary and will fully respect standard practices, including participants' informed consent. The proposal places a greater emphasis on enhanced care and support using specialist and tertiary care resources in a more focused way. Once fully operational, the pilot project will cost about \$20 million per year.

It is estimated that more than 12,000 people in B.C. are living with HIV, and approximately 27 per cent of these individuals remain undiagnosed.

Highly active antiretroviral therapy (HAART), introduced in 1996 at the Vancouver International Conference on AIDS, is considered the 'gold standard' for treatment of HIV, and was in large part driven by groundbreaking, internationally recognized work at the BC Centre for Excellence in HIV/AIDS. Today's pilot project commitment will facilitate access to life-saving HAART drugs for at-risk populations.

"We have made great strides in HIV/AIDS treatment, allowing individuals to live longer lives," said Dr. Montaner. "The challenge we face now is reaching out to individuals who would otherwise fall between the cracks and cannot access treatment. This program is aimed at bringing the treatment to the people in need. I want to thank Premier Campbell for his leadership and commitment to this important and innovative initiative."

"Dr. Julio Montaner is a recognized international leader, who is passionate about the care, treatment and support of HIV infected persons. We are fortunate to have him lead the BC Centre for Excellence in HIV/AIDS," said Premier Campbell. "Because of their work right here in B.C., people's lives around the world are changed for the better."

At an individual level, HAART treatment slows disease progression, extends life expectancy, and significantly reduces the number of new AIDS-related diseases and HIV-related deaths. At a population level, the BC Centre for Excellence in HIV/AIDS has provided strong evidence that treatment of people living with HIV in a given jurisdiction can also dramatically decrease the transmission of the disease.

Mathematical modelling suggests that this pilot project in these two regions could avert as many as 173 HIV infections in the first five years, which in turn represents about \$65 million in avoided lifetime HIV treatment costs alone.



Premier Gordon Campbell and Dr. Julio Montaner



The 2nd Global Experts Summit

The 2nd Global Experts Summit: Leading by Example in the Public Health Approach to Antiretroviral Therapy (ART) took place from February 11 to 13, 2009. The Summit was co-organized by the World Bank and Global Fund to Fight AIDS, Tuberculosis and Malaria and co-hosted by the BC Centre for Excellence in HIV/AIDS (BC-CfE) and the Public Health Agency of Canada (PHAC).

The Summit objectives were designed to build on the success of the widespread implementation of ART programs in resource-limited settings over the past several years.

This Summit was in many ways a continuation of the 2008 World Health Organization (WHO) AIDS Conference, which built broader engagement and an understanding of the urgent need to advocate for and invest in an operations research agenda to help strengthen delivery of HIV interventions. While the public health approach recommended by WHO has helped to rapidly expand access to ART in some of the poorest regions of the world, it has also raised clinical, programmatic and health systems questions regarding how to maximize the impact of these programs. The Summit sought to find answers to these questions.

In addition to the stakeholders represented at the 2008 WHO consultation, the Vancouver Summit included representation from eight research-based pharmaceutical companies: Abbott, Boehringer-Ingelheim, Bristol-Myers Squibb Foundation, Gilead, GlaxoSmithKline, Merck, Schering-Plough and Tibotec.



Dr. Pedro Cahn, M.D.,
past president of the IAS

Content experts from multilateral organizations, the research community, civil society, donor agencies, the medical community and the pharmaceutical industry delivered presentations on five topic areas: maximizing the positive impact of ART on prevention; ART initiation; optimization of ART drug regimens; monitoring of ART; and program implementation and health systems strengthening. Discussions and breakout groups following these presentations allowed participants to develop a series of recommendations for action.

Theme 1: Maximizing the Positive Impact of ART on Prevention

Reuben Granich (Medical Officer in the Department of HIV/AIDS, World Health Organization) gave the keynote presentation on ART as a prevention modality that addressed community viral load rather than individuals' pre- or post-exposure health.

The WHO modelling study recently published in *The Lancet* suggests that annual universal, voluntary testing, immediately followed by ART for all who test positive, regardless of CD4+ count or viral load, could eliminate HIV infection. This strategy would lead to marked reductions in morbidity, mortality and HIV incidence with a favourable cost-benefit impact. The model projects an estimated 95 per cent incidence reduction in 10 years.

Guidelines/recommendations include:

- ART guidelines should consider the added potential preventive impact of expanding ART coverage. For instance, the IAS-USA guidelines note that treatment should be considered at any CD4 count for the HIV-positive member of a sero-discordant couple.
- From a public health perspective, reducing community viral load should be a key target of ART roll-out.

Theme 2: ART Initiation

Julio Montaner (President of the IAS and director of the BC Centre for Excellence in HIV/AIDS) discussed new evidence regarding the optimal time to start ART, including the new 2008 IAS-USA and US Department of Health and Human Services (DHHS) guidelines. These guidelines recommend starting ART before CD4 counts drop to below 350/mm³, and even starting when counts are above 350/mm³ if there is evidence of high viral load, rapid CD4 decline, or co-morbidities (including chronic hepatitis B or C infection, increased cardiovascular risk, underlying renal disease, etc.) that may be adversely affected by inflammatory events resulting from ongoing HIV replication.

Deferring ART until patients have CD4/mm³ counts of 200 is no longer desirable as this is associated with increased morbidity and mortality. In fact, recent data from the Strategies for Management of Antiretroviral Therapy (SMART) indicates that at all stages of HIV infection, ongoing viral replication leads to disseminated intravascular inflammation and clotting which, in turn, leads to end-organ dysfunction. This process is proportional to the plasma viral load, and it is irrespective of CD4 count. Furthermore, ongoing inflammation is an important driver of non-AIDS related morbidities, such as cardiovascular events, liver dysfunction, nephropathy and malignancies.

Guidelines/recommendations include:

- ART should be initiated earlier, with strong evidence suggesting ART be started at CD4 cell count above 350/mm³.
- Regimens need to be well tolerated, safe, robust and convenient.
- The role of nevirapine as first-line drug of choice should be revisited.
- Adherence support should be stressed, including travel support, and food support.
- Consider promoting viral load monitoring.
- ART should be initiated in everyone with tuberculosis, irrespective of CD4 cell count.
- ART should be offered to all HIV-positive pregnant women.
- The safety of efavirenz in pregnancy should be urgently revisited.

Theme 3: Optimization of ART Drug Regimens

Pedro Cahn (Director, Fundacion Huesped, Buenos Aires, Argentina, and former IAS President) gave the keynote address. He suggested that first-line regimens with good tolerability and efficacy should be promoted, with second-line regimens provided in a timely fashion. He also highlighted the need for close monitoring of treatment and the need to integrate ART programs within the health system.

Cahn also emphasized the importance of addressing pediatric treatment issues, as children are often diagnosed late in HIV infection, have limited access to appropriate pediatric formulations and suffer high rates of morbidity and mortality as a result.



Dr. Julio Montaner and Craig McClure, Executive Director of the IAS

Guidelines/recommendations include:

- Treatment safety and tolerability should be a key consideration in choosing drug regimens.
- Triomune (a combination of d4T, 3TC and zidovudine) should no longer be the global normative drug combination.
- More optimal first-line regimens, especially boosted protease inhibitor-based regimens should be included, and the role of novel drug classes should be considered.
- Raltegravir should be optimally used in second-line or salvage regimens with a boosted protease inhibitor.
- Multiple regimens and more options for clinicians should be part of normative agency guidance.
- Atripla (a combination of tenofovir, FTC and efavirenz) is to be recommended as a preferred initial therapy option.

Theme 4: Monitoring of ART

Elly Katabira (Associate Dean for AIDS Research, Department of Medicine, Makerere University and President-elect of the IAS) gave the keynote address, and emphasized that intensified and improved ART monitoring is required to achieve optimal outcomes. He underscored a number of issues endemic to resource-limited settings and their monitoring strategies, such as the fact that they do not account for variation in the health-seeking behaviour of patients, and that they involve inadequate and expensive laboratory services and unreliable drug supply.

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A number of changes could help improve monitoring. For instance, counselling could help address adherence and behaviour change. Clinical evaluation should include assessing ART complications and new or worsening opportunistic infections. And laboratory monitoring should include CD4+ count and viral load monitoring at least once per year.

In addition, Katabira suggested that clinical monitoring, adherence profiling and CD4 testing should be used to prioritize viral load monitoring needs, with operations research being conducted to refine criteria regarding who should have a viral load test when resources are limited.

Guidelines/recommendations include:

- Viral load monitoring should be included in normative agency guidance.
- Cheaper and more accessible viral load tests need to be developed for better clinical monitoring.
- Drug resistance testing at point-of-care and population-level resistance surveillance should be used to help guide appropriate drug regimens.
- Adherence monitoring should include data collection of early warning indicators (appointment-keeping, drug pickup, pill-counting, etc.) to help guide clinical monitoring among ART programs.
- Guidance on adherence monitoring should be included in overall clinical guidance.

Theme 5: Program Implementation and Health Systems Strengthening

Jim Yong Kim (Division of Social Medicine and Health Inequalities, Brigham and Women's Hospital, Department of Social Medicine, Harvard Medical School) gave the keynote address and highlighted the need for HIV prevention and treatment to be integrated into primary care. He emphasized the challenge of the "implementation bottleneck," which may actually tighten if underlying issues affecting weak health systems are not addressed as part of the global response. He recommended an interdisciplinary approach to assess health system dynamics that includes a business analysis at the clinical- and system-level, the development of case studies and simulation models, hypothesis-driven research, creation of a design delivery model, implementation and evaluation.

He noted that – unlike in the clinical field – there is no normative framework for health system design; the HIV field needs to know how particular implementation strategies and program designs lead to desired outcomes, positing a new 'science of health care delivery' that would address how best to deliver a health intervention to everyone.

No guidelines/recommendations were established for this content area. However, precursors to establishing recommendations were identified:

- Information systems capacity must be strengthened to monitor ART impact (including developing indicators, a minimum data set, data generation and standardized reporting systems and data use protocols).
- Generic protocols need to be established to measure the impact of HIV management on the health care workforce, drug supply chain and other components of the health system.



Content experts from multilateral organizations, the research community, civil society, donor agencies, the medical community and the pharmaceutical industry delivered presentations.

Dr. Julio Montaner receives the LifeSciences BC Leadership Award

Dr. Julio Montaner received the prestigious Leadership Award at the recently held 11th Annual LifeSciences BC Awards.

Founded in 1991, LifeSciences BC supports and promotes British Columbia's world-class life sciences and biotechnology sectors. The Annual LifeSciences BC Awards have come to be known as the premier event to celebrate the outstanding successes of B.C.'s life sciences community.

Dr. Montaner was recognized for his many years of outstanding leadership, both nationally and internationally, in curbing the growth of HIV and AIDS around the world. His work was acknowledged to have furthered treatment strategies that have been responsible for saving countless lives and improving quality of life for people with HIV/AIDS.

"This is truly a special moment for me," said Dr. Montaner. "I am very proud of the work we do at the BC Centre for Excellence in HIV/AIDS and am honoured to be recognized by such eminent members of B.C.'s research community. I share the honour of this award with my colleagues, whose endless dedication to the highest standards of patient care has made a difference in the lives of so many."

Dr. Montaner was one of the original leaders in the development of modern highly active antiretroviral therapy (HAART). He has also played an important role in the evaluation of simplified HAART regimens, and pioneered multiple drug rescue therapy. A tireless campaigner for better access to therapy, he has pioneered the notion that increasing access to antiretroviral drugs will have a profound effect on decreasing progression to AIDS and death among those infected, and will similarly decrease HIV transmission rates among those at risk.

Dr. Montaner has also been instrumental in the rapid transfer of research advances into clinical practice through B.C.'s HIV/AIDS therapeutic guidelines.

Dr. Simon Pimstone, chair of LifeSciences BC, singled out the BC Centre for Excellence in HIV/AIDS (BC-CfE) for high praise. Dr. Pimstone said the BC-CfE had significantly contributed to the province's reputation for innovation by conducting cutting-edge research that has had a major impact on the delivery of health care. "How we treat patients with HIV/AIDS has always been informed by innovative research,



Dr. Julio Montaner accepted the Leadership Award at the Awards Gala on April 8, 2009.

both at the laboratory bench as well as at the bedside, and Dr. Montaner and his colleagues at the BC-CfE are internationally recognized pioneers in the field," Dr. Pimstone said.

He also acknowledged the importance of the BC-CfE's HIV/AIDS research to world science, especially its research on the preventive properties of HAART. "HAART has been amongst the finest examples of innovation in modern medicine," said Dr. Pimstone. "In just two decades, HIV/AIDS has been transformed from a death sentence to a treatable chronic disease, and this advance has been made possible to a large extent by the BC-CfE's research efforts and their ability to incorporate these into the Standard of Care."

Dr. Pimstone pointed out that B.C.'s biotechnology industry has become a major force in the province's current economic prosperity. While B.C. has historically relied on natural resources for much of its wealth, it is those regions that nurture and promote their intellectual and scientific resources which will benefit from the tremendous opportunities offered by a new global age.

"The world economy is set to double in the next 20 years," Pimstone observed. "That's twice as much business as today, twice as many opportunities, as people—particularly from Asia, South America and eastern Europe—become consumers for the first time, start taking modern medicines, establishing bio-based

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crops to feed communities, and deploying new forms of greener energy to power the vehicles of tomorrow.”

In his opening address during the awards ceremony, Pimstone emphasized the importance of government support for the life sciences, urging the Province to make science and technology a priority. He also praised key initiatives such as the Conversation on Health and the establishment of the Pharmaceutical Task Force as recent examples of the government’s commitment to these areas.

The Premier’s recent announcement of funding for a BC-CfE-proposed five-year pilot project expanding access to HAART in some of the province’s most impoverished communities is the most recent example of this commitment, not only to the health and well-being of British Columbians, but also to the province’s wealth of talented and dedicated medical scientists and practitioners.



Dr. Simon Pimstone singled out the BC-CfE for high praise at the LifeSciences BC Awards.



Dr. Viviane Dias Lima

Dr. Viviane Dias Lima honoured with a Young Investigator Award

Dr. Viviane Dias Lima, senior statistician at the BC Centre for Excellence in HIV/AIDS (BC-CfE), received a Young Investigator Award at the 16th Conference on Retroviruses and Opportunistic Infections (CROI), held in February 2009. CROI is a scientifically focused meeting of the

world’s leading researchers working to understand, prevent and treat HIV/AIDS and its complications.

Dr. Lima was recognized for her work in identifying discrepancies between the Amplicor and the Taqman assays to measure viral load. She measured the number of patients whose viral counts were detectable with the Taqman assay and found that they had doubled over those captured with the Amplicor assay. Her work received a great deal of attention at the Montreal meeting as it has far-reaching implications for treatment and research.

The BC-CfE has shared this information with regulatory agencies in Canada and the U.S., as well as with the manufacturer, in an attempt to use this information to develop a corrective strategy.

Her paper will be published in an upcoming issue of the *Journal of Acquired Immune Deficiency Syndromes*.

Dr. Lima’s current research is extensive. She is conducting several studies aimed to characterize the impact of adherence to different highly active antiretroviral therapy (HAART) regimens on outcomes. She is involved in the mathematical modelling of universal access to HAART as part of a comprehensive HIV prevention strategy. She is also working on a mathematical model focused on South Africa, which models incidence and prevalence rates of HIV among different risk groups in that country.



Drug trade involvement among street-involved youth

Werb D, Kerr T, Li K, Montaner J, Wood E

Street-involved youth have been shown to be involved in the street-level illicit drug trade in a number of jurisdictions, though little is known about risk factors and causes of this behaviour. This study was conducted to investigate factors associated with this activity.

Researchers used logistic regression to examine factors associated with drug-dealing among participants in the At-Risk Youth Study (ARYS) in Vancouver. They also examined motivations for drug trade involvement and types of drugs sold by participants.

The study followed 529 street-involved youth during the study period, of whom 58% reported having been involved in the drug trade in the last six months. In a logistic regression analysis, crack cocaine use (Adjusted Odds Ratio [AOR] = 1.84, 95% CI: 1.28–2.67), homelessness (AOR = 1.58, 95% Confidence Interval (CI): 1.04–2.40), and having been assaulted by police (AOR = 1.85, 95% CI: 1.14–3.00) were independently associated with drug-dealing among cohort participants. Among participants who reported drug-dealing, 85.6% of individuals stated that the main

reason that they sold drugs was to pay for their personal drug use.

Street-involved youth implicated in the drug trade had drug-related and socio-demographic vulnerabilities, seemed motivated by drug dependence and reported police violence—findings which have immediate implications for drug strategies targeting street-level drug dealing.

(The American Journal of Drug and Alcohol Abuse)

Sexually transmissible infections among street-involved youth

Marshall B

This paper reviews research on the individual and contextual factors that influence street youth sexual behaviour, and analyzes their potential impact on HIV and sexually transmitted infections (STIs).

The review focuses on street youth research conducted in North America; studies from other high-income countries were included where relevant for comparative analysis. Although much research examining the epidemiological basis for their heightened susceptibility has concentrated on the individual behaviours and characteristics associated with acquiring these infections, contextual factors, including the social, structural and environmental forces that

influence sexual risk behaviour, are increasingly found to play an important role in shaping the transmission dynamics of HIV and STIs within these marginalized populations.

Research areas reviewed include the psychosocial determinants of sexual risk behaviour, substance use and sexual activity, social and peer-group influences on sexual activity, sexual activity and the physical environment, and structural factors and sexual risk activity.

Hypothetical strategies, outlined in the literature, for reducing vulnerabilities among street youth are also reviewed.

(Culture, Health and Sexuality)

Methamphetamine injection, hepatitis C infection and street-involved youth

Miller C, Kerr T, Fisher B, Zhang R, Wood E.

Hepatitis C is a serious health issue for street-involved youth. This study was conducted to determine factors associated with hepatitis C virus (HCV)-antibody-positive status among street-involved youth.

A total of 519 street-involved youth were included in these analyses, among whom 152 (29%) were female and 124 (24%) were Aboriginal. The median age was 22 years. In total, 66 participants (13%) were HCV-

antibody-positive at baseline, and 219 reported injection drug use (42%). Injection drug use was the strongest predictor for being HCV-antibody-positive, with 30% of youth who injected drugs testing positive for the antibody. Injection drug users injected heroin and crystal methamphetamine at least once daily.

Previous research has shown that young people in this setting were more likely to inject heroin than older people who inject drugs, but were less likely to access methadone maintenance therapy. This study underscores the vulnerability of heroin-dependent youth to blood-borne infection and a corresponding need for methadone treatment programs aimed at this vulnerable population.

Results indicate the need to avert a widespread HCV epidemic by ensuring that street-involved youth have access to harm reduction services, including needle exchanges, and that service providers, including the police, are supportive of their participation.

(Journal of Adolescent Health)

BC-CfE research assistant receives award



An HIV/AIDS care outreach initiative in Uganda.

Katie Muldoon has been awarded a Simon Fraser University Graduate International Research Travel Award, in the amount of \$6,250, through the Senate Graduate Awards Adjudication Committee.

This will support the work she is doing with David Moore in Uganda for the Highly Active Antiretroviral Therapy (HAART) as Prevention Project. She will study the effect of HAART treatment as prevention among sero-discordant couples living in Jinja, Uganda. This study will

directly contribute to the global effort to reduce the spread of HIV and will build research capacity for high quality HIV prevention research in both Canada and Uganda.

Ms. Muldoon is a research assistant at the BC-CfE, working with Eric Druyts, epidemiologist, in the field of epidemiology and population health. She has worked in research environments in both Canada and Africa and looks forward to further developing her experience in Uganda.

what's new

Updated Adult Therapeutic Guidelines now available

The most recently updated *Adult Therapeutic Guidelines* are now available to download in PDF format on the BC-CfE website at www.cfenet.ubc.ca.

The guidelines are a consensus of the Centre's Therapeutic Guidelines Committee. This information represents the committee's interpretation of current treatment of HIV/AIDS and related conditions. The guidelines are reviewed biannually and form the basis of treatment strategies for HIV/AIDS care practitioners across B.C.

What's new welcomes event submissions from all HIV/AIDS-related agencies. Please e-mail submissions to info@cfenet.ubc.ca

The 8th International Conference on Urban Health (ICUH)

Nairobi, Kenya
October 18-23, 2009

Call for abstracts: The 2009 International Conference on Urban Health (ICUH) brings together the leaders of urban health research and practice, along with community voices, to provide clear insight and offer direction and best practices towards healthy urbanization. The conference is planned around three components: The Scientific Program, an Urban Health Champions Forum and a Community Voices Forum. Organizers invite the submission of abstracts online at www.icuh2009.org, where a full outline of themes and sessions can be found along with detailed submission guidelines.

BC Centre for Excellence in HIV/AIDS

- > Improve the health of British Columbians with HIV through comprehensive research and treatment programs;
- > Develop cost-effective research and therapeutic protocols;
- > Provide educational support programs to health-care professionals;
- > Monitor the impact of HIV/AIDS on B.C. and conduct analyses of the effectiveness of HIV-related programs.

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