

 This presentation will discuss the expansion of HAART as a powerful strategy to reduce not only AIDS and HIV related morbidity and mortality, but also reducing HIV transmission and therefore HIV incidence.

The case for expanding access to highly active antiretroviral therapy to curb the growth of the HIV epidemic

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• We first outlined the case for expanding HAART to curb the growth of the epidemic in 2006 in a landmark Lancet paper. While controversial at the time, our proposal has now been widely endorsed by key opinion leaders as well as international AIDS organizations, including IAS, WHO, and UNAIDS.

Lancet 2006; 368: 531-36

The case for expanding access to highly active antiretroviral therapy to curb the growth of the HIV epidemic



• The fundamental concept is that HAART stops HIV replication. Shortly after a patient starts antiretroviral therapy, viral replication shuts down.

• Typically it takes between 6 and 9 months for plasma viral load (pVL) to become undetectable, depending on pVL prior to initiation of HAART. Thereafter, the amount of virus in tissues and other bodily fluids, including sexual fluids also begins to decrease.

• The principle driver of transmission is the amount of virus transmitted in bodily fluid from one person to another. Therefore, decreasing the amount of virus in bodily fluid will reduce the risk of transmitting the virus.



• The role of ART in prevention first became apparent in the setting of Vertical Transmission.

• Prior to 1996, vertical transmission rates were between 30 and 50%.

• Since 1996, there has been a rapid decline in vertical transmission rate due to antiretroviral therapy.

• In fact, there have been only two documented cases of HIV infected newborns in BC over the last five year. These cases were as a result of system failures as opposed to treatment failures.



• More recently, a meta analysis was conducted to evaluate the impact of HAART on sero-discordant heterosexual couples (i.e. one partner is HIV positive and the other partners is HIV negative).

• A 92% reduction in HIV transmission was seen in serodiscordant couples in which the HIV positive partner was on antiretroviral therapy.

Longitudinal community plasma HIV-1 RNA concentrations and incidence of HIV-1 among injecting drug users: prospective cohort study

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• In North America and parts of Europe injection drug use (IDU) is a significant driver of HIV transmission. The nature of transmission in the IDU population is different (i.e. the amount of blood transmitted is often substantial). As a result, it is important to explore whether treatment can have a preventive effect in this setting.

• This study investigated the community pVL and the rate of new infections among injection drug users in Vancouver's Downtown Eastside (DTES).

Longitudinal community plasma HIV-1 RNA concentrations and incidence of HIV-1 among injecting drug users: prospective cohort study

ENE 16 MAY 2009 | VOLUME 338



• Between 1996 and 1999, we documented a dramatic decrease in the median community viral load in the DTES due to the introduction of HAART. Longitudinal community plasma HIV-1 RNA concentrations and incidence of HIV-1 among injecting drug users: prospective cohort study

BMI | 16 MAY 2009 | VOLUME 338



• This was associated with a parallel effect in the reduction of HIV incidence among IDUs in the DTES.

• Using statistical methods we were able to show that the community viral load at baseline (before the introduction of HAART) was a stronger determinant (by a factor of 10) than the risk associated with sharing needles.



• We then investigated the impact of HAART at the population level.

- Between 1996 and 1999 there was a greater than 40% decrease in HIV rates in BC.
- HIV incidence remained stable between1999 and 2004.



• The fact that the HIV rates decreased despite rising rates of syphilis after 1996 suggest that the decrease in HIV rates are not likely due to safer sex practices.



- · We then used the same data to estimate the cost-effectiveness of HAART
- Prior to 1996 there were approximately 800 cases per year

• After the initial rollout of HAART in BC, HIV cases decreased to 400 per year



• The most conservative estimate of the total cost of medical management of 1 HIV infection over a lifetime is \$ 250,000

• In 2005, 400 cases of HIV were averted (i.e. new cases decreased from about 800 to 400 – see previous slide)

• In 2005 we spent about \$50 Million on HAART to treat nearly 4,000 patients in BC. A cost effective initiative by itself.

• In addition, at the prevention level \$100 Million Rx costs were averted



Incremental net benefit (Millions of CDN \$) over 30 years

K Johnston et al.

AIDS, 2010

Overall population and patient-centered incremental net benefit associated with immediately increasing HAART from 50 to 75% and measuring costs and benefits over a simulated period of 30 years, based on a willingness-to-pay threshold of US\$ 50000 per quality-adjusted life year.

• In a separate study we investigated the economic impact of a given expansion of HAART coverage in BC.

We evaluated the incremental net benefit (Millions of CDN \$) over 30 years

• The patient-centered incremental net benefit (dashed curve) becomes flat after a couple of decades, this implies that there is a ceiling on the return on investment.

• In contrast, the overall population impact (solid curve), which adds the preventive benefit of HAART on HIV transmission, shows a rather exponential increase of the return on investment over time. This is because subsequent generations of HIV infections are aborted.



AIDS Nov 27th 2008, The Economist Deploying the drugs used to treat AIDS may be the way to limit its spread



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• The upcoming slides will discuss the experiences related to HAART in BC.



• This slide shows the natural expansion of HAART over the past 10 years.

• Between the summer of 1996 to 2000, approximately 2,500 individuals were placed on HAART .

• Between 2000 and 2004, we reached a steady state, largely due to concerns regarding HAART related toxicities.

• In 2004, new guidelines were established and, therefore, the number of individuals on HAART increased by about 2,500 between 2004 and 2009.

Improved Virological Outcomes in British Columbia Concomitant with Decreasing Incidence of HIV Type 1 Drug Resistance Detection



• Here we see that over the last 15 years the rate of plasma viral load suppression has been increasing (bottom graph), while the rate of acquired resistance has declined (top graph). Note that the latter is shown using a semi-log scale, and therefore, we are showing a >90% decrease in acquired resistant in BC over the same period.

• The impact of a fully funded province wide HAART program has been remarkably successful in the BC setting.



Figure 1: Number of active HAART participants and number of new HIV diagnoses peryear in British Columbia, Canada, 1996–2009 p values are for trend and were obtained from the generalised additive model. Injecting drug user (IDU) refers to individuals who have ever injected illicit drugs. HAART=highly active antiretroviral therapy. BC=British Columbia. NA=not available.

• Here we see a negative correlation between the number of people on HAART and new HIV diagnoses. More HAART equals less new HIV diagnoses.



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• On phase 2, between 2000-2004, new HIV diagnoses were stable, and this was associated with a stable number of people on HAART.



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• In the third phase, between 2004-2009, the number of people on antiretroviral therapy increased significantly and similarly, HIV new diagnoses decreased significantly.



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• The green line are the number of new HIV infections among IDUs.

• New HIV diagnoses within IDUs did not significantly decline until a few years ago when Vancouver Coastal Health mobilized an intensive campaign to engage this population into care. As a result, we have seen approximately 50% decrease in new HIV cases among IDUs over the last three years in BC.



• This graph depicts the frequency distribution of the plasma viral load in BC, in order to better understand the opportunities available to increase treatment and prevention strategies.

• The number of people living with HIV has grown over time, however, at the same time, the number of people who have a detectable plasma viral load remains stable, and in fact the number of people with a high detectable plasma viral load (dark blue) has declined.

• Obviously, we have a unique opportunity to intervene by reengaging individuals who have detectable plasma viral load. Whether it is initiating treatment for the first time or changing treatment options, the goal is to suppress their viral load to ensure that they derive the full benefit of HAART, and in doing so to decrease community viral load to further reduce HIV transmission.

 Another crucial part of the strategy includes to increase testing in the general population, including populations considered to be at relative low risk, so that we can identify the approximately 25% of individuals who are HIV positive have not been diagnosed.



• The changes in HIV new diagnoses showed earlier have taken place against a background of steady or rising STI and HCV.



IAS-USA Guidelines 2010: When to Start

Asymptomatic Infection	Recommendation
 CD4+ cell count < 500 cells/mm³ 	Start HAART
 CD4+ cell count > 500 cells/mm³ 	Should be considered*
Initiation of Therapy Recommended Regardless of CD4+ Cell Count	
Symptomatic HIV disease	
Acute Opportunistic Infection	
Pregnant Women	
 Older than 60 yrs of age 	
 HIV-1 RNA > 100,000 copies/mL 	
 CD4+ cell count Decline >100 cells/mm³/yr 	
Active HBV or HCV	
 Active or High Risk for Cardiovascular Disease 	
 HIV-Associated Nephropathy 	
 Symptomatic Primary HIV infection 	
 Sero-discordant couples (or High Risk of HIV Transmission) 	
*Unless pt is elite controller or has stable high CD4+ count and low HIV-1 RNA off ART	
Thompson M, Aberg J, Cahn P, Montaner J, et al. JAMA. 2010;304;321-333	

The new International AIDS Society-USA guidelines are a lot more liberal than in the past.
Basically they now recommend HAART be initiated in most HIV infected individuals regardless of CD4 cell count, except for are elite controllers.

• Please note that the older than 60 years, has now been revised to older than 50 years.

• The BC CfE is in the processes of developing guidelines for BC, which will closely reflect the above guidelines.



- Combination prevention therefore is part of the solution.
- Although this presentation focused on HIV testing and linkage to care and HAART, the importance of other interventions and of using all of our evidence-based arsenal in a combined prevention approach is vital.



antiretroviral treatment in stopping new infections and how it can be effectively used as part of combination HIV prevention approaches must be further explored, as shown by Dr Julio Montaner, President of the International AIDS Society.

Our proposed approach has now been endorsed by UNAIDS, as the cornerstone of the global fight against HIV/AIDS.



Treatment as prevention serves as the basic founding block for the new UNAIDS strategy, named Treatment 2.0



AIDS still kills 2m people a year. But the rate of new infections is falling and it is possible to imagine bringing the disease under control



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