Expanding HAART to Stop HIV & AIDS

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Professor of Medicine and Chair, AIDS Research, University of British Columbia
President, International AIDS Society
Vancouver 1996
“One World One Hope”
Montaner et al JAMA, March 25th 1998

Triple Therapy: AZT + ddI + NVP

Gulick et al; JAMA, July 1, 1998

% Progression to AIDS in 3 yrs

Vancouver 1996
“One World One Hope”
Impact of HAART in BC-CfE

Death Rate per 1000

Life Expectancy at age 20

Hogg et al. Unpublished; 2009
Impact of HAART in BC-CfE

Median CD4 Cell Count > 350/mm³

Median Plasma Viral Load < 50 copies/mL

Hogg et al. Unpublished; 2009
Prevention Strategies

- Education
- Change in behaviour
- Harm reduction
- New strategies/technology
- Vaccines
Prevention Strategies

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*Existing strategies have failed to contain the global HIV pandemic*
The case for expanding access to highly active antiretroviral therapy to curb the growth of the HIV epidemic

Julio S G Montaner, Robert Hogg, Evan Wood, Thomas Kerr, Mark Tyndall, Adrian R Levy, P Richard Harrigan

“The upshot of this widespread failure to recognize that AIDS is an exceptional crisis and threat is that the response to the pandemic is not made commensurate to the challenges—and so the epidemic escalates even while it erodes our capacities to check it.”

Dr Peter Piot, UNAIDS Executive Director

International AIDS Society
Stronger Together

AIDS 2006
Time to Deliver
HAART Can Reduce HIV Transmission

HAART stops HIV replication

↓

HIV levels fall to undetectable in blood as well as sexual fluids

↓

Sharp reduction in HIV transmission
Canada: Infants Exposed to HIV and Born HIV Positive

Number of infants exposed to HIV mothers

Number of infants born HIV positive
Discordant Couples

Rx of index case

No Rx | pre-HAART | HAART

Impact of HAART in BC-CfE

J Montaner et al, EIDJ, under review, 2009
Impact of HAART in BC-CfE

Plasma Viral Load ($\log_{10}$ copies/mL) Distribution

- 24 months
- Baseline

J Montaner et al, EIDJ, under review, 2009
Cost of Medical Management of 1 HIV infection over a lifetime = $250,000

HIV deficit in BC in 2005: 400

Cost-Effectiveness of HAART BC-DTP

Averted lifetime Rx cost up to 2001 US $96.4M

A total of 3,963 pts were on HAART in BC in 2005

Total actual drug cost (using patented drugs) in 2005 $49 million US

800 cases per year

400 cases per year

“HIV deficit” in BC in 2005: 400
Cost-Effectiveness of HAART BC-DTP

“HIV deficit” in BC in 2005: 400

Cost of Medical Management of 1 HIV infection over a lifetime = $250,000

Averted lifetime Rx cost up to U$A 100M
A total of 3,963 pts were on HAART in BC in 2005
Total actual drug cost (using patented drugs) in 2005
U$A 50M
Expected Impact of an Increase in HAART Coverage from current 50 to 75% of Medically Eligible on New HIV Infections in BC

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

- **Baseline = Status Quo**
- **Scenario I = Incremental Benefit going from Baseline to 50% coverage with Expanded Eligibility (n=761)**
- **Scenario II = Added Incremental Benefit going from Scenario I to 75% coverage Expanded Eligibility (n=1187)**

- Net benefit is an economic measure that incorporates survival and QoL

- 1 Quality adjusted life year (QALY) valued at $50K

* All Values discounted at 3% per year, using 2005 CDN$
Summary

- HAART is widely regarded as a cost effective, life-saving strategy
  - Mortality of treated HIV/AIDS patients
  - Morbidity of treated HIV/AIDS patients
  - Health Resource utilization
  - Vertical Transmission of HIV infection

- Furthermore, when the impact of HAART on HIV transmission is considered, HAART expansion becomes a **cost-averting** strategy
Integrating HIV Prevention and Treatment from Slogans to Impact

HIV Incidence and AIDS Mortality among Adults in Sub-Saharan Africa, 2003–2020, under Different Intervention Scenarios

J Salomon¹*, D Hogan¹, J Stover², K Stanecki³, NWalker³-⁴, P Ghys³, B Schwartländer⁵

**STOP HIV & AIDS**

**Seek and Treat to Optimally Prevent HIV & AIDS**

**Intervention**
HAART Expansion within current guidelines

**Primary Endpoint**
HIV Incidence*

**3 years**

**Secondary Endpoints:**
- mortality and morbidity
- HIV-1-RNA Levels
- HIV resistance
- CD4 cell counts
- adverse events and safety labs
- hospitalizations
- resource utilization
- adherence to HAART

*Primary analysis = HIV incidence pre-HAART expansion vs year 3*
**STOP HIV & AIDS**

 Seek and Treat to Optimally Prevent HIV & AIDS

<table>
<thead>
<tr>
<th>HAART Coverage*</th>
<th>Reduction of HIV Transmission</th>
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<tbody>
<tr>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>30-40%</td>
<td>50%</td>
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<tr>
<td>50-60%</td>
<td>XX%</td>
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*Among all those infected with HIV*
Expansion of HAART for HIV Prevention: Remaining Challenges

 ✓ Untested hypothesis
 ✓ Safety/toxicity
 ✓ Individual rights
 ✓ Resistance
 ✓ Hidden epidemics
 ✓ Logistics
 ✓ Erosion of prevention effort
 ✓ Cost
Expansion of HAART for HIV Prevention: Remaining Challenges

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- Erosion of prevention
- Cost

However, we are currently proposing to evaluate the impact of expanding HAART on HIV transmission by increasing coverage WITHIN THOSE IN MEDICAL NEED!

WHO 2008: This hypothesis must be urgently tested!
Expansion of HAART for HIV Prevention

- A Perfect Storm
  - New Guidelines
  - BC-AIDS related Mortality
Antiretroviral Treatment of Adult HIV Infection
2008 Recommendations of the International AIDS Society–USA Panel

Scott M. Hammer, MD
Joseph J. Eron Jr, MD
Peter Deeks, MD, PhD
Robert T. Schooley, MD
Melanie A. Thomassen, MD
Sharon Waldron, MD
Pedro Cali, MD
Margaret A. Flesh, MD
Jean M. Kawell, MD, PhD
Martin S. Hirsch, MD
Dona M. Jacobson, BS
Julian S. Montaner, MD
Douglas D. Richman, MD
Patrick G. Yonk, MD
Paul A. Volberding, MD

Context: The availability of new antiretroviral drugs and formulations, including drugs in new classes, and recent data on treatment choices for antiretroviral-naive and -experienced patients warrant an update of the International AIDS Society–USA guidelines for the use of antiretroviral therapy in adult human immunodeficiency virus (HIV) infection.

Objectives: To summarize new data in the field and to provide current recommendations for the antiretroviral management and laboratory monitoring of HIV infection. This report provides guidelines in key areas of antiretroviral management, including how to initiate therapy, choice of initial regimen, patient monitoring, and how to change therapy and how best to approach treatment options, including optimal use of recently approved drugs (once-daily, pill-free, and oral), in treatment-experienced patients.

Data Sources and Study Selection: A 14-member panel with expertise in HIV research and clinical care was appointed. Data published or presented at selected scientific conferences since the last panel report (August 2006) through June 2008 were identified.

Data Extraction and Synthesis: Data that changed the previous guidelines were reviewed by the panel (according to section). Guidelines were drafted by section writing committees and were then reviewed and edited by the entire panel. Recommendations were made by panel consensus.

Conclusions: New data and considerations support initiating therapy before CD4 cell count declines to less than 350/µL. In patients with ≥350 CD4 cells/µL, or more, the decision to begin therapy should be individualized based on the presence of comorbidities, risk factors for progression to AIDS or non-AIDS disease, and current readiness for treatment. In addition to the prior recommendation that a high plasma viral load (eg, >100,000 copies/mL) and rapidly declining CD4 cell count (>100/µL per year) should prompt treatment initiation, active hepatitis B virus infection, cardiovascular disease risk, and HIV-associated nephropathy increasingly prompt earlier therapy. The initial regimen must be individualized, particularly in the presence of co-morbid conditions, but usually will include efavirenz or a ritonavir-boosted protease inhibitor plus 2 nucleoside reverse transcriptase inhibitors (tenofovir/abacavir or stavudine/lamivudine), with other co-medications considered to minimize drug interactions and drug toxicity, and potentially allow for a normal life span.

The rationale for the current update of the 2006 International AIDS Society–USA guidelines is discussed in detail in this report.
SMART: Consequences of Stopping HAART

**Change in D-Dimer (µg/mL) From Baseline to 1 Month**


**Change in IL-6 (pg/ml) From Baseline to 1 Month**

*P* = .0005 for trend

## When to Start HAART

<table>
<thead>
<tr>
<th>Symptomatic HIV disease</th>
<th>Therapy recommended</th>
<th>Recommendation strengthened since 2006</th>
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### CD4 <350/µL
- Therapy recommended

### CD4 >350/µL
- Therapy should be considered and decision individualized

### Correlates of faster HIV disease progression:
- High viral load (>100,000c/mL)
- Rapidly declining CD4 (>100/µL per year)

### Coexistent conditions influenced by uncontrolled viremia:
- Presence of, or high risk for, cardiovascular disease
- Active HBV or HCV
- HIV-associated nephropathy
- Pulmonary Hypertension

### Examples
Costs associated with an expanded drug program may seem high initially, said Abbott. But he said the strategy needs to be considered on a long-term basis.

“It’s far more cost-effective to prevent disease than it is to treat disease,” he said.
Until there is a vaccine, Mr. Clinton said, studies show that suppressing blood levels of HIV with potent antivirals can help block the disease's transmission. The Chair of AIDS Research at the University of British Columbia, Julio Montaner, who is the incoming president of the International AIDS Society that sponsors this conference, is a leading champion of using drugs as preventatives.
The third approach, though, is the most intriguing. This is to do nothing more than press ahead faster with the treatment program. Since treatment reduces viral load, it should, in theory, make those being treated less infectious. Of course, theory is one thing and practice another. But studies in Taiwan and British Columbia (the latter by Julio Montaner, the incoming president of the International AIDS Society, which organizes the conference) have shown big falls in transmission rates as ARVs have been rolled out.
The Power of HAART: Demographic Model

Montaner et al, Lancet 2006
Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model

Deploying the drugs used to treat AIDS may be the way to limit its spread.

**Plan:** Test 100% yearly and treat 100% of those testing HIV+.

**Expected Results:** The rate of new infections (now 20/1,000 people per year) would fall within 10 years of full implementation to 1/1,000 per year. Within 50 years the prevalence of HIV would drop below 1%, compared with up to 30% at the moment in the worst-affected areas.
STOP HIV & AIDS
Seek and Treat to Optimally Prevent HIV & AIDS


BC-MoH
Sutherland Foundation & 625 Powell Foundation
Pharmaceutical Industry
MSHRF and CIHR-CTN
PHAC, H&W, Ottawa
NIDA, NIH

Research Staff and Study Participants

British Columbia Centre for Excellence in HIV/AIDS

St. Paul’s Hospital