Test & Treat - Using Treatment as Prevention

Julio Montaner MD, DSc(hon), FRCPC, FCCP, FRSC, OBC
Director, BC-Centre for Excellence on HIV/AIDS, Providence Health Care
Professor of Medicine and Head, Division of AIDS, University of British Columbia
Past-President, International AIDS Society
Learning Objectives

Upon completion of this presentation, participants should be better able to:

- Characterize the secondary preventive value of HAART as it relates to decreasing HIV transmission

- Identify approaches to enhance the secondary preventive value of HAART as it relates to decreasing HIV transmission

Note: This presentation does not include discussion of any non-FDA-approved or investigational use of any product/device.
Vancouver 1996
“One World One Hope”
Montaner J et al. JAMA. 1998

Triple Therapy: AZT + ddI + NVP

AZT + ddI

AZT + NVP

Study Weeks

Montaner J et al. JAMA. 1998

Vancouver 1996
“One World One Hope”

% Progression to AIDS in 3 yrs


CD4+/µL

HIV-1 RNA Difference From Baseline, log Copies/mL

Duration of Treatment, wk

Triple Therapy: AZT + ddI + NVP


Dual Therapy Regimens

Triple Therapy: AZT + ddI + NVP

Change in Viral Load

Study Weeks

Plasma HIV RNA (thousand copies/mL)

> 750

501-750

351-500

201-350

< 200
Impact of HAART in BC-CfE

- **Death Rate per 1000**: Decreasing trend from 1993-94 to 2003-04.
- **Life Expectancy at age 20**: Increasing trend from 1993-94 to 2003-04.

Modified from Hogg et al, Lancet. 2009
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
AIDS 2006
XVI International AIDS Conference
Time to Deliver
HAART stops HIV replication

↓

HIV load falls to undetectable levels in plasma

as well as in sexual fluids

↓

Sharp reduction in HIV transmission
Prevention Strategies

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

*Existing strategies have failed to contain the global HIV pandemic*
Canada: Infants Exposed to HIV and Born HIV Positive

Modified from www.phac-aspc.gc.ca/aids-sida/publication/index-eng.php#surveillance
# Impact of ART Sero-discordant Heterosexual Couples

S. Attia, M. Egger, M. Muller, M. Zwahlen and N. Lowa. AIDS. 2009 Jul 17;23(11):1397-404

92% reduction in HIV Transmission Risk from 5.64 to 0.46 transmissions per 100 person-years

<table>
<thead>
<tr>
<th>HIV-1 RNA copies/mL</th>
<th>No. of studies</th>
<th>No. of events</th>
<th>No. of person years</th>
<th>Rate (95% CI)</th>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>&lt;400</td>
<td>2</td>
<td>0</td>
<td>291</td>
<td>0.0 (0-1.27)</td>
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<tr>
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<td>1</td>
<td>0</td>
<td>52</td>
<td>0.0 (0-5.79)</td>
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<td>5</td>
<td>1098</td>
<td>0.46 (.19-1.09)</td>
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<tr>
<td>Not on ART</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>&lt;400</td>
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<td>1</td>
<td>631</td>
<td>0.16 (.02-1.13)</td>
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<td>457</td>
<td>2.06 (5-7.47)</td>
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<tr>
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<td>18</td>
<td>456</td>
<td>4.17 (.84-20.65)</td>
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<tr>
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<td>47</td>
<td>668</td>
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<tr>
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<td>5</td>
<td>48</td>
<td>534</td>
<td>9.03 (3.87-21.09)</td>
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<tr>
<td>All studies</td>
<td>10</td>
<td>456</td>
<td>9998</td>
<td>5.64 (3.28-9.70)</td>
</tr>
</tbody>
</table>
3408 heterosexual HIV discordant couples from 7 African countries

349 (10%) HIV partners started therapy

Followed for up to 24 months

92% reduction in HIV transmission
Longitudinal community plasma HIV-1 RNA concentrations and incidence of HIV-1 among injecting drug users: prospective cohort study


Whiskers represent 95% confidence intervals.
Longitudinal community plasma HIV-1 RNA concentrations and incidence of HIV-1 among injecting drug users: prospective cohort study


- **Median Viral Load** (10,000 copies per mL)
- **HIV Incidence Rate** (per 100 person years)

Whiskers represent 95% confidence intervals.
Decline Community Viral Load is strongly associated with HIV incidence among IDUs

Gregory Kirk, ..., David Vlahov for the Alive Cohort, CROI 2011
New HIV in BC

Rate per 100,000 population


HIV

Modified from M Rekart, BC-CDC, 2006
New HIV and Syphilis in BC

Rate per 100,000 population

HIV
Syphilis

Modified from M Rekart, BC-CDC, 2006
Cost-Effectiveness of HAART
BC-DTP

“HIV deficit” in BC in 2005: 400

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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$A 50M
Overall population and patient-centered incremental net benefit associated with immediately increasing HAART from 50 to 75% and measuring costs and benefits over a simulated period of 30 years, based on a willingness-to-pay threshold of US$ 50,000 per quality-adjusted life year.

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

K Johnston et al, AIDS, 2010
MEXICO CITY -- Former U.S. President Bill Clinton, fresh from a tour of his foundation's projects in Africa, took the stage of the International AIDS Conference here to tell thousands that "we must do more."

"AIDS is a big dragon," Mr. Clinton said Monday, but unlike the mythical dragon slain by St. George, "this dragon must be slain by millions and millions of foot soldiers."

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

HIV prevalence

Cost of treatment

Number of infections prevented

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

Universal Voluntary Testing and Treatment for Prevention of HIV Transmission

Carl W. Dieffenbach, PhD
Anthony S. Fauci, MD

JAMA, June 10, 2009—Vol 301, No. 22

Research Issues

- Universal testing
- Relationship of the stage of HIV infection to efficiency of transmission
- Efficacy of ART in preventing HIV transmission
- Drug resistance
- Behavioral “disinhibition”
- Benefit to the individual
- Cost-effectiveness for society
Deploying the drugs used to treat AIDS may be the way to limit its spread.
Deploying the drugs used to treat AIDS may be the way to limit its spread.
Expanding HAART Coverage in BC within the evolving IAS-USA Therapeutic Guidelines
Figure 1: Number of active HAART participants and number of new HIV diagnoses per year 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.
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Figure 3: Distribution of yearly pre-HAART CD4 cell counts for all individuals initiating HAART in British Columbia, Canada, 1996–2009. HAART = highly active antiretroviral therapy.
Improved Virological Outcomes in British Columbia Concomitant with Decreasing Incidence of HIV Type 1 Drug Resistance Detection

Vikram S. Gill,1 Viviane D. Lima,1,2 Wen Zhang,1 Brian Wynhoven,1 Benita Yip,1 Robert S. Hogg,1,3 Julio S. G. Montaner,1,2 and P. Richard Harrigan1,2

CID 2010:50 (1 January) • HIV/AIDS

Acquired resistance falling

Plasma viral load suppression rising
HIV testing in BC, 1985 to 2008

<table>
<thead>
<tr>
<th>Year</th>
<th># of HIV Tests</th>
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<tbody>
<tr>
<td>1994</td>
<td>104,229</td>
</tr>
<tr>
<td>1995</td>
<td>129,941</td>
</tr>
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<td>1996</td>
<td>137,980</td>
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<td>140,092</td>
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<td>2006</td>
<td>172,058</td>
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<tr>
<td>2007</td>
<td>176,224</td>
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<td>2008</td>
<td>182,151</td>
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</tbody>
</table>
Hepatitis C, 1999-2008

- BC
- Canada

2004

Infectious Syphilis, 1999-2008

- BC
- Canada

2004

Genital Chlamydia, 1999-2008

- BC
- Canada

2004

Gonorrhea, 1999-2008

- BC
- Canada

2004

“Provincial Viral Load”
All Patients Ever Tested for Plasma HIV-1-Viral Load in BC

Censoring at the time of Death or Move

Montaner et al, Lancet, 2010
Decreases in Community Viral Load Are Accompanied by Reductions in New HIV Infections in San Francisco.


doi:10.1371/journal.pone.0011068

n=12,512 unduplicated HIV-positive individuals.
HIV+ tests by region by year

Modified from PHAC, Feb 2011
The spectrum of engagement in HIV care in the United States spanning from HIV acquisition to full engagement in care, receipt of antiretroviral therapy, and achievement of complete viral suppression. We estimate that only 19% of HIV-infected individuals in the United States have an undetectable HIV load.
Combination prevention

**HIV Prevention**

- **Biomedical Interventions**
  - HIV testing, linkage to care and expanded HAART coverage

- **Structural Interventions**

- **Community Interventions**

- **Individual and small group behavioral interventions**

Modified from T. Coates
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.

Dr Montaner’s study, published in the *Lancet*, was the strongest confirmation yet that treatment and prevention are two sides of the same coin. The study showed that the annual rate of infection in 1996—the year when the modern regime of highly active antiretroviral therapy (HAART) was introduced—had, by 2009, fallen by 52%. During that period the number of people on treatment rose by 547%.
In Collaboration with VCHA, NHA, PHSA, Community, MHL&S and MHS

Supported through a $48M (+ drugs) four year outreach grant by BC Government, $2.5M five year Avant Garde Award by the National Institute for Drug Abuse (NIDA) at the NIH in 2008, a $110K CIHR grant $48M and grants from Merck, Gilead and ViiV