TREATMENT AS PREVENTION®
From Research Hypothesis to Global Policy and Beyond

Julio Montaner, OC, OBC, MD
Professor of Medicine and Head, Division of AIDS, University of British Columbia
Director, BC Centre for Excellence in HIV/AIDS at Providence Health Care
UNAIDS Special Advisor on HIV Therapeutics

Hosted by Bruce Gamage
Provincial Infection Control Network of BC

USA – Trends in Annual Rates of Death
Men - Ages 25-44

* Ages 25 to 44

US-CDC, 1997

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INCAS Trial

- Dual therapy: ZDV + NVP
- Dual therapy: ZDV + DDI
- Triple therapy: ZDV + DDI + NVP


Merck 035

- AZT + 3TC
- Indinavir
- AZT + 3TC + IDV

Conclusions In most HIV-infected patients with prior antiretroviral therapy, the combination of indinavir, zidovudine, and lamivudine reduces levels of HIV RNA to less than 500 copies per milliliter for as long as one year. (N Engl J Med 1997;337:734-9.)

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April

November

Vancouver 1996
“One World One Hope”

Impact of HAART in BC

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New HIV and Syphilis in BC

![Graph showing rates of HIV and Syphilis in BC from 1991 to 2004.](image)

BCCDC, 2005

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THE LANCET

Viewpoint

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

*Lancet* 2006; 368: 531–36

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Increasing HAART Coverage in BC

Baseline CD4 count by year in BC

Montaner et al, PLOS One 2014

Modified from Montaner et al, PLOS One, Feb 12th 2014

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Longitudinal adherence to HAART, by refill compliance, in BC

ARV Drug Resistance in BC

Modified from Montaner et al, PLOS One, Feb 12th 2014
Plasma HIV-RNA levels in BC
(all HIV + individuals)

Modified from Montaner et al, PLOS One, Feb 12th 2014

The Cascade of Care over time in BC

Modified from Nosyk et al, Lancet ID, Jan 2014

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AIDS Incidence in BC

Mortality among HIV infected People in BC

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## Mortality & Life Expectancy in BC

<table>
<thead>
<tr>
<th>Mortality rate (95%CI) per 1000 person-years</th>
<th>Life expectancy at age 20 years (standard error)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003 - 2005 33.76 (29.41 – 38.57)</td>
<td>28.82 (1.82)</td>
</tr>
<tr>
<td>2009 - 2012 18.22 (14.57 – 22.50)</td>
<td>49.81 (1.69)</td>
</tr>
</tbody>
</table>

Mother to Child Transmission (MTCT)

ART is virtually **100% effective** at preventing MTCT

Over the last 15 years, with the widespread use of ART, MTCT has been virtually eliminated in BC

- 2 HIV+ newborns in **300** HIV+ pregnancies
- Both cases failed to use ART (**diagnosed at labour**)
- Expected with no HAART > **30 cases**
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Modified from Montaner et al, PLOS One, Feb 12 2014

Modified from Montaner et al, PLOS One, Feb 12th 2014

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Drug Resistance in BC

Year

% Suppressed

% With Resistance


Phylogenetic Mapping of HIV in BC
Harrigan, Poon, Joy, et al.
Hosted by Bruce Gamage
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An ‘actionable’ cluster

- Detected growth of a cluster by 11 new cases in 3 months.
- 8 new cases carried transmitted HIV drug resistance* (TDR).
- Prompted a formal outbreak investigation by provincial health agency.

*K103N, NNRTI resistance

Expanding ART Saves Lives and Money
(e.g.: South Africa)

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HPTN 052: Effectiveness of Treatment as Prevention

Immediate vs. Delayed ART in Sero-Discordant Couples

HR = 96.3% reduction in transmission
No difference whether index patient was Male or Female

Hosted by Bruce Gamage
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HPTN 052: SUSTAINABILITY OF TasP

- No linked HIV transmissions when index participant stably suppressed on ART

- 8 linked HIV infections diagnosed after seropositive pt started ART
  - 4 infections likely occurred before, or soon after, ART initiation, and 4 infections occurred after ART failure in seropositive pt

- Unlinked partner infection rates similar between study arms

Cohen MS, et al. IAS 2015. Abstract MOAC0101LB.
A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa

The TEMPRANO ANRS 12136 Study Group®

Baseline Characteristics

<table>
<thead>
<tr>
<th>CD4+ count — cells/mm³</th>
<th>Median</th>
<th>460</th>
<th>459</th>
<th>467</th>
<th>466</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Interquartile range</td>
<td>359–560</td>
<td>364–575</td>
<td>369–584</td>
<td>394–572</td>
</tr>
<tr>
<td>CD4+ count stratum — no. (%)</td>
<td>≥500 cells/mm³</td>
<td>201 (39)</td>
<td>212 (41)</td>
<td>222 (43)</td>
<td>214 (41)</td>
</tr>
<tr>
<td></td>
<td>350–499 cells/mm³</td>
<td>189 (37)</td>
<td>193 (38)</td>
<td>188 (37)</td>
<td>211 (41)</td>
</tr>
<tr>
<td></td>
<td>&lt;350 cells/mm³</td>
<td>121 (24)</td>
<td>107 (21)</td>
<td>105 (20)</td>
<td>93 (18)</td>
</tr>
</tbody>
</table>

Plasma HIV-1 RNA — log₁₀ copies/ml

| Median | 4.6 | 4.6 | 4.7 | 4.7 |
| Interquartile range | 4.0–5.2 | 4.0–5.3 | 4.0–5.3 | 4.0–5.3 |

TEMPRANO ANRS 12136 Study Group, N Engl J Med. 2015

TEMPRANO: Immediate vs Deferred ART ± IPT

30-Mo Probability, %

- Deferred ART: 14.1
- Deferred ART + IPT: 8.8
- Immediate ART: 7.4
- Immediate ART + IPT: 5.7

Cumulative Probability of Death or Severe HIV-Related Illness (%)

Mos From Randomization

TEMPRANO ANRS 12136 Study Group, N Engl J Med. 2015

Hosted by Bruce Gamage
www.webbertraining.com
START: Immediate ART Reduced Risk of Serious Events or Death by 57%

- 4.1% vs 1.8% in deferred vs immediate arms experienced serious AIDS or non-AIDS–related event or death (HR: 0.43; 95% CI: 0.30–0.62; \( P < .001 \))

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PrEP in Randomized Clinical Trials

<table>
<thead>
<tr>
<th>TDF/FTC oral PrEP</th>
<th>PROUD *</th>
<th>IPERGAY</th>
<th>Partners PrEP</th>
<th>TDF2</th>
<th>iPrEx</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2015, n=523</td>
<td>2015, n=400</td>
<td>2011, n=1579</td>
<td>2011, n=1210</td>
<td>2010, n=2499</td>
</tr>
<tr>
<td></td>
<td>58</td>
<td>86</td>
<td>89</td>
<td>40</td>
<td>55</td>
</tr>
<tr>
<td></td>
<td>44</td>
<td>67</td>
<td>81</td>
<td>44</td>
<td>62</td>
</tr>
</tbody>
</table>

Efficacy (with 95% confidence interval)

Updated from J Montaner, JAMA 2014.

New Directions in the 2015 Consolidated ARV Guidelines Update

Meg Doherty, MD, PhD, MPH
19 July 2015
WHO Satellite
Vancouver – IAS 2015

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antiretroviral therapy (ART) should be initiated in everyone living with HIV at any CD4 cell count. Second, the use of daily oral pre-exposure prophylaxis (PrEP) is recommended as a prevention choice for people at substantial risk of HIV infection.
AMBITIOUS TREATMENT TARGET

THE FINAL CHAPTER OF THE AIDS EPIDEMIC

Ambitious Treatment Target by 2020

90% diagnosed
90% on treatment
90% virally suppressed

THE FINAL CHAPTER OF THE AIDS EPIDEMIC

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Ending AIDS: Reducing new infections and AIDS-related deaths by 90% of 2010 levels

Stover et al. GAP Report, UNAIDS, 2014

Progress toward the 90-90-90 Target in BC as % of Estimated HIV Prevalence


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Progress toward the 90-90-90 Target in BC
as % of previous step


UN General Assembly
Sept 25th 2014

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Ensure healthy lives and promote well-being for all at all ages
3.3: By 2030, end the epidemics of AIDS, tuberculosis, malaria & neglected tropical diseases. Combat hepatitis, water-borne diseases & other communicable diseases

“...To cut new infections in half, we’ll have to heed Julio Montaner’s years of pleas to implement Treatment as Prevention... We can save a lot of lives if all this is done...”

President Clinton
International AIDS Conference
Washington 2012

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“Treatment 2.0: A new prevention–treatment paradigm in the global response to HIV/AIDS
UNGASS New York – 6 June 2011”

“ZERO NEW INFECTIONS–TREATMENT FOR EVERYONE WHO NEEDS IT
LETTER TO PARTNERS | 2010

“The role of 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.”
Michel Sidibé
Executive Director, UNAIDS

“Few could have imagined that we’d be talking about the real possibility of an AIDS-free generation. But that’s what we’re talking about ... make no mistake, we are going to win this fight.”
President Obama, Dec 1, 2011

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UNAIDS and Caritas — Expansion of Antiretroviral Therapy Consultation.
Rome, February 25th 2014

“I can communicate with delight that currently, with the help of friends and with the collaboration of the local Church and civil institutions, we are about to start a project of ‘Test and Treat’ in the District of Shinyanga, in Tanzania, which aims to guarantee antiretroviral treatment to more than 120,000 people over five years.”

S.E. Archbishop Zygmunt Zimowski,
President of the Pontifical Council for Health Care Workers

Vatican City, March 10th–11th, 2015

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SECRETARIAT OF STATE

No. 64.781

From the Vatican, 5 June 2015

Dear Dr. Montaner,

His Holiness Pope Francis thanks you for informing him of the forthcoming International Conference on HIV/AIDS in Vancouver. He sends pious greetings to all taking part, and expresses his interest for their work and the dedication it requires.

His Holiness is grateful for the many advances made in the prevention and treatment of HIV/AIDS, particularly through Highly Active Antiretroviral Therapy, and the promotion of “Treatment through Prevention”. The lives that have been saved, both through the reduction in the number of new infections and the better health and longer lifespans of those already diagnosed, give witness to the possibilities for beneficial outcomes when all sectors of society unite in common purpose. He hopes that further efforts may be made to make the fruits of research and medicine available to the world’s poorest people, especially orphaned children, upon whom this scourge often places the heaviest burden. He likewise prays that all advances in pharmacology, treatment and research will be matched by a firm commitment to promote the integral development of each person as a beloved child of God. Upon all of you, the Holy Father invokes always divine blessings of wisdom and peace.

With every good wish, I am

Yours sincerely,

Peter Land, P.P.
Secretary of State

October 8, 2015

Dr. Julio I.G. Montaner:

nearest and Chief, CDC Division of AIDSug

BC Cancer, Vancouver, British Columbia

I am especially pleased in our dialogue with you and am sure this year to develop this shared and quality care.

Sincerely,

Judy O. Trachten
Leader of the Liberal Party of Canada

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The Economist

The end of AIDS?
How 5 million lives have been saved, and a plague could now be defeated

Treatment as Prevention

Targeted Disease Elimination

Health Care Sustainability

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December 10  RISING TO THE CHALLENGE OF MULTIDRUG-RESISTANT GRAM-NEGATIVE RODS (CRE & FRIENDS)
Dr. Jonathan Otter, King’s College, London

December 17  (FREE Teleclass)
EXAMINING THE “UNMENTIONABLES” = SANITATION AND THE GLOBAL AGENDA
Rose George, Author & Journalist

www.webbertraining.com/schedulept1.php

JUST OVER THE HORIZON ...