INTERNATIONAL
HIV TREATMENT
AS PREVENTION
WORKSHOP

From Evidence to Action: The 2nd International HIV Treatment as Prevention Workshop
April 22-25, 2012
www.treatmentaspreventionworkshop.org

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Past-President, International AIDS Society
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National Institutes of Health
Office of AIDS Research

National Institute of Allergy and Infectious Diseases

Bill & Melinda Gates Foundation

anR5

French National Agency for Research on AIDS and Viral Hepatitis

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A place of mind
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Canada: Infants Exposed to HIV and Born HIV Positive
Partners for the Prevention of HSV/HIV Transmission Study: Discordant Couples

- Prospective cohort analysis (n=3408 heterosexual HIV discordant couples)
- 7 African countries
- 349 HIV+ initiated HAART
- 103 Linked HIV transmissions
  - Only 1 while on HAART. Adjusted incidence rate ratio 0.08% (0.00-0.57; P=0.004)
- Sexual risk behaviors decreased after HAART 6.2% vs 3.7% (P=0.03)
- No change in sexual frequency

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

- From 1997, HIV incidence decreased by 74% for each log decline in community HIV viral load.
- In a separate model, HIV incidence decreased by 5% for each 1% increase in HAART coverage.

Modified from G Kirk et al, for the Alive Cohort, CROI 2011
Increasing HAART Coverage within Evolving Guidelines in BC - Impact on New Diagnoses

TasP Workshop 2012 (Updated from Montaner et al, Lancet, 2010)
Combination HIV Prevention

- Education
- Condoms
- STI treatment
- Testing/counseling
- Treatment as prevention
- Male circumcision
- Microbicides
- Drug/alcohol treatment
- PMTCT
- PrEP
- Harm reduction
More evidence on the way: TasP Relevant Studies

*Current HIV Research, 2011, 9, 355-366*
Gupta, Granich et al: Timeline for Selected TasP studies

Figure includes studies with an available timeline—others not listed.
HPTN 052: Immediate vs Delayed ART in Sero-discordant Couples

- **Deferred**
  - HR = 96.3% reduction in transmission
  - No difference whether index pt was M or F

- **Immediate**

HPTN 052: Immediate vs Delayed ART in Sero-discordant Couples

Extra-Pulmonary TB
Deferred: 17 cases
Immediate: 3 cases
84% Reduction

M Cohen et al, IAS-Rome, July 2011
M Cohen, NEJM 2011
The end of AIDS?

How 5 million lives have been saved, and a plague could now be defeated
Aids - is the end really in sight?

US Secretary of State Hillary Clinton has offered to lead the end-stage of the battle against Aids - but will the money be forthcoming to finish the job and deliver an "Aids-free generation"?

Three Key Pillars:

MC
MTCT
TasP

The Guardian, UK
Nov 8th 2011

US secretary of state Hillary Clinton has urged the United States and other nations to increase their funding for HIV/Aids prevention and treatment. Photograph: Win McNamee/Getty Images
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, December 1, 2011

By the end of 2013, PEPFAR will directly support more than 6 M people on HAART—2M more than previously targeted.

Ambassador Eric Goosby, TasP Workshop 2012
HIV Treatment as Prevention

On 1 December, George Washington University in Washington, D.C., hosted “The Beginning of the End of AIDS,” a splashy World AIDS Day event that featured three U.S. presidents, business magnates, and rock stars. The catalyst that brought them together was something Anthony Fauci, the top U.S. government HIV/AIDS scientist, told the crowd even 1 year ago would have seemed “wishful thinking”: a clinical trial dubbed HPTN 052 and its “astounding” result.

HIV/AIDS researchers have long debated whether antiretroviral drugs (ARVs)
# Treatment Discordant Couples in 2011

<table>
<thead>
<tr>
<th>ART</th>
<th>No. couples</th>
<th>Person-year observed</th>
<th>No. HIV new infections</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>18,371</td>
<td>13366.2</td>
<td>151</td>
<td>1.13</td>
</tr>
<tr>
<td>No</td>
<td>16,158</td>
<td>12195.9</td>
<td>305</td>
<td>2.50</td>
</tr>
<tr>
<td>Total</td>
<td>35,016</td>
<td>25562.1</td>
<td>456</td>
<td>1.78</td>
</tr>
</tbody>
</table>

**ART reduce 55% transmission in 2011**

Z Wu, TasP Workshop 2012
Treatment as Prevention: Effect of ART Coverage on HIV Incidence in Rural South Africa

- Annual population-based HIV surveillance in rural KwaZulu-Natal 2004 to 2011
- 1395 HIV seroconversions among 16,588 HIV-negative adults ≥15 years of age

Spatial Estimates of Proportion of HIV Patients on ART

Adjusted HIV Infection Rate by ARV Coverage Category

Majority of HIV Transmissions From People Unaware of Their Infection

- ~21% unaware of their infection
- ~79% aware of their infection

Account for ~54% of new infections

Account for ~46% of new infections

People Living With HIV/AIDS (1,039,000-1,185,000)

New Sexual Infections Each Year (~48,000)

Spectrum of Engagement in care - USA

- HIV-infected: 1,178,350
- HIV-diagnosed: 941,950
- Linked to HIV care: 725,302
- Retained in HIV care: 480,395
- On ART: 426,590
- Suppressed viral load (≤200 copies/mL): 328,475

Source: MMWR © 2011 Centers for Disease Control and Prevention (CDC)
SAN FRANCISCO’S APPROACH TO MAXIMIZING THE CONTINUUM OF PREVENTION, CARE AND TREATMENT

HIV Surveillance

Test → Diagnosis → Primary Care → Treatment → Virologic Suppression

Primary Prevention Efforts
- PrEP, PEP, condoms, syringes
- Drivers
  1. Substance use
  2. Alcohol
  3. Meth
  4. Crack
  5. Poppers
  6. STDs, # of partners

LINCS: Linkage, Navigation & Retention Team

↑ Routine Medical Testing
↑ Community Testing
↑ Linkage & Partner Services

Mental Health Services
Substance Use Treatment
Housing Support

Treatment Adherence
Medical Case Management
ART Guidelines Uptake
STD & PCSI
Engagement & Partner Services
**IAS-USA Guidelines: When to Start**

<table>
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<tr>
<th>CD4+ Cell Count</th>
<th>Recommendation</th>
</tr>
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<tr>
<td>&lt; 350 cells/mm³</td>
<td>Start ART (AI)</td>
</tr>
<tr>
<td>350-500 cells/mm³</td>
<td>Start ART (AII)</td>
</tr>
<tr>
<td>&gt; 500 cells/mm³</td>
<td>Start ART (BIII)</td>
</tr>
</tbody>
</table>

**Clinical Conditions Favoring Initiation of Therapy Regardless of CD4+ Cell Count**

- History of AIDS-defining illness (AI)
- Pregnancy (AI)
- HIV-associated nephropathy (AII)
- HBV co-infection (AII)
- Patients at risk of transmitting HIV to sexual partners (AI, heterosexuals; AIII, others)
- HCV co-infection* (BII)
- Patients > 50 years of age (BIII)

*Offer ART to all HIV infected patients unless patient is elite controller or has stable CD4+ count and low HIV-1 RNA in absence of ART.*

DHHS, 2012: When to Start

ART recommended for all HIV-infected patients

**strength** of recommendation varies according to CD4+ cell count

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*Including those with high CD4 count and/or with cirrhosis. If CD4> 500/mm³ may elect to defer ART until after HCV therapy

• **Rating of Recommendations:** A = Strong; B = Moderate; C = Optional
• **Rating of Evidence:** I = data from RCTs; II = data from well-designed nonrandomized trials or cohort studies with long-term clinical outcomes; III = expert opinion

DHHS Guidelines for Antiretroviral Therapy in Adults and Adolescents. March 27, 2012.
WHO Guidance on couples HIV testing and counselling, including antiretroviral therapy for treatment and prevention in serodiscordant couples

5. HIV-Positive partners with >350 CD4 cells/μL in serodiscordant couples should be offered ART to reduce HIV transmission to uninfected partners. *Strong recommendation, high quality evidence.*

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**RECOMMENDATIONS**

1. Couples and partners should be offered voluntary HIV testing and counselling with support for mutual disclosure. *Strong recommendation, low-quality evidence.*

2. Couples and partners in antenatal care settings should be offered voluntary HIV testing and counselling with support for mutual disclosure. *Strong recommendation, low-quality evidence.*

3. Couples and partner voluntary HIV testing and counselling with support for mutual disclosure should be offered to individuals with known HIV status and their partners. *Strong recommendation, low-quality evidence for all people with HIV in all epidemic settings / Conditional recommendation, low-quality evidence for HIV-negative people depending on country-specific HIV prevalence.*

4. People with HIV in serodiscordant couples and who are started on antiretroviral therapy (ART) for their own health should be advised that ART is also recommended to reduce HIV transmission to the uninfected partner. *Strong recommendation, high-quality evidence.*

5. HIV-positive partners with >350 CD4 cells/μL in serodiscordant couples should be offered ART to reduce HIV transmission to uninfected partners. *Strong recommendation, high-quality evidence.*

Antiretroviral prophylaxis: a defining moment in HIV control

<table>
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<tr>
<th>Study</th>
<th>Effect size (95% CI)</th>
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<tbody>
<tr>
<td>Antiretroviral treatment for prevention</td>
<td>96% (73–99)</td>
</tr>
<tr>
<td>HPTN 052 Africa, Asia, Americas(^5)</td>
<td></td>
</tr>
<tr>
<td>PrEP for discordant couples</td>
<td>73% (49–85)</td>
</tr>
<tr>
<td>Partners PrEP Uganda, Kenya(^1)</td>
<td></td>
</tr>
<tr>
<td>PrEP for heterosexual men and women</td>
<td>63% (21–84)</td>
</tr>
<tr>
<td>TDF2 Botswana(^7)</td>
<td></td>
</tr>
<tr>
<td>Medical male circumcision</td>
<td>54% (38–66)</td>
</tr>
<tr>
<td>Orange Farm, Rakai, Kisumu(^6,8)</td>
<td></td>
</tr>
<tr>
<td>PrEP for MSMs</td>
<td>44% (15–63)</td>
</tr>
<tr>
<td>iPrEX Americas, Thailand, South Africa(^4)</td>
<td></td>
</tr>
<tr>
<td>Sexually transmitted diseases treatment</td>
<td>42% (21–58)</td>
</tr>
<tr>
<td>Mwanza Tanzania(^10)</td>
<td></td>
</tr>
<tr>
<td>Microbicide</td>
<td>39% (6–60)</td>
</tr>
<tr>
<td>CAPRISA 004 South Africa(^1)</td>
<td></td>
</tr>
<tr>
<td>HIV vaccine</td>
<td>31% (1–51)</td>
</tr>
<tr>
<td>RV144 Thailand(^13)</td>
<td></td>
</tr>
</tbody>
</table>

*Figure: HIV prevention technologies shown to be effective in reducing HIV incidence in randomised controlled trials\(^3,11\)*

PrEP=Pre-exposure prophylaxis. \(^*\) Meta-analysis of circumcision trials.
Expanding ART for Treatment and Prevention of HIV in South Africa: Estimated Cost and Cost-Effectiveness 2011-2050

Granich et al. PLoS One February 2012 | Volume 7 | Issue 2 | e30216
TasP Works, So Let’s Start Planning for Implementation

Jose M Zuniga, Other, 10:01AM May 2, 2012

The workshop’s bottom-line messages:

- TasP works in combination with other prevention interventions
- Additional research is needed, without which some will have grounds to dispute TasP
- While research continues, planning for TasP implementation must start now
- HIV testing uptake and linkages to TasP and treatment as treatment must improve
- The health workforce requires training and support to implement TasP
- TasP must count on community acceptance and requires community ownership
- HIV-positive patients require treatment literacy and should not be coerced into treatment without truly informed consent

In less than three months, 30,000-plus global AIDS warriors will gather in Washington, DC, for the XIX International AIDS Conference. Several TasP studies will report out at this year’s conference – which will infuse the conference with the same spirit of optimism that permeated Vancouver almost two decades ago. Our challenge is to turn optimism into action!
All Scientific work is incomplete – whether it be observational or experimental. All scientific work is liable to be upset or modified by advancing knowledge. That does not confer upon us a freedom to ignore the knowledge we already have, or to postpone the action that it appears to demand at a given time.

Austin Bradford Hill (1897-1991) British epidemiologist best known for his research with Richard Doll, which linked smoking with lung cancer. He was also widely acknowledged as the world’s leading medical statistician and a pioneer in the use of RCTs.