HIV-1 Transmission: Treat to Prevent? 
...and HPTN 052

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Transmission of HIV-1

Biological Requirements

Infectious

- Inoculum (concentration)
- Phenotypic factors

Susceptibility

- Hereditary resistance
- Innate resistance
- Acquired (immune) resistance
Treatment as Prevention

“The Four Questions”

• Can ART prevent HIV transmission?  
  - magnitude and durability

• What do we tell infected people?

• Can we reduce HIV incidence with ART?

• Barriers to “Treatment as Prevention”?
Stable, healthy, serodiscordant couples, sexually active
CD4 count: 350 to 550 cells/mm³

Primary Transmission Endpoint
Virally linked transmission events

Primary Clinical Endpoint
WHO stage 4 clinical events, pulmonary tuberculosis, severe bacterial infection and/or death
HPTN 052 Timeline: NOT (!!!) The Fast Track

• ART for prevention of HIV 1993 – THE PRESENT
Establishing HIV treatment as prevention in the HIV Prevention Trials Network 052 randomized trial: an ethical odyssey

Myron S Cohen\textsuperscript{a}, Marybeth McCauley\textsuperscript{b} and Jeremy Sugarman\textsuperscript{c}
HPTN 052 Enrollment
(Total Enrollment: 1763 couples)

- U.S. 278
- Americas
- Brazil
- Botswana
- South Africa
- Africa 954
- Thailand
- India
- Kenya
- Malawi
- Zimbabwe
- Asia 531

Total Enrollment: 1763 couples
Results of the HPTN052 trial announced on 12 May 2011 show that if an HIV-positive person adheres to an effective antiretroviral therapy regimen, the risk of transmitting the virus to their uninfected sexual partner can be reduced by 96%.

“Treatment for prevention is a game changer”.

Michel Sidibe
Executive Director of UNAIDS
HPTN 052: Effect of ART

Proportion of participants with VL<400 at each visit

- Immediate Arm
- Delayed Arm (not on ART)
- Delayed Arm (on ART)

Months: 0 3 6 9 12 15 18 21 24 27 30 33 36 39 42 45
What Happened Next?
The Economist

The end of AIDS?

How 5 million lives have been saved, and a plague could now be defeated

June 4, 2011
HPTN 052: What Happened Next

- All HIV infected subjects offered ART
  - 1682 index cases/1763 (96% retention)
  - 1502 discordant couples (85% retention)
  - 1561/1682 index cases are NOW on ART

DURABILITY OF PREVENTION?
DELAYED ART & CLINICAL OUTCOMES
Acceptance of ART in Delay Arm

- **May 2011**
  - Began informing participants of interim study results

- **January 2012**
  - 802 (94%) of active Index Cases in delay arm notified
    - 209 (26%) already on ART, met CD4 threshold before May 2011
    - 424 (53%) had accepted ART
    - 169 (21%) had declined ART

- **June 2012**
  - 70 more delay Index Cases have initiated ART
Acceptance of ART in Delay Arm

In Jan 2012, why did 21% of participants decline ART?

- 53% not ready to begin ART
- 21% believe their CD4 is too high
- 16% planning to begin at later times
- 4% still deciding
- 2% wanting to discuss with family/friends
- 4% other
HPTN 052 and IAS 2012

- Ken Mayer: Sexual Behavior?
- Beatrice Grinjzstein: When to Start?
- Rochelle Walensky: Cost Effective?
- Ying Chen: Progression of HIV?
HPTN 052 and Public Policy
HIV Treatment As Prevention: How Scientific Discovery Occurred And Translated Rapidly Into Policy For The Global Response

ABSTRACT In 2011 interim results of HIV Prevention Trials Network study 052, a National Institutes of Health study designed to test the effectiveness of antiretroviral treatment against the spread of HIV, were reported. These results showed that in a stable relationship in which one member of the couple was infected with HIV, treatment of the infected partner with antiretroviral drugs, combined with couples counseling and condom use, resulted in a 96 percent reduction in sexual transmission of HIV-1. This finding led to the use of antiretroviral treatment as a cornerstone of HIV prevention. Independent advisory committees of the President’s Emergency Plan for AIDS Relief (PEPFAR) and the World Health Organization (WHO) have since issued analyses that set the stage for broader use of antiretroviral agents in treatment and prevention. This article describes the separate PEPFAR and WHO recommendations and outlines the design of prospective new trials to test how best to maximize the benefits of early treatment for prevention.
PEPFAR and HPTN 052

- Treat HIV before CD4 count falls below 350
- Treat HIV immediately in pts. with TB
- Endorse WHO PMTCT guidelines
- Earlier treatment at higher CD4 counts
  -highest risk patients including couples
- Program for special populations
- Seek more investment
WHO, HPTN 052 and Couples

www.who.int/hiv/pub/guidelines/9789241

- Couples should be provided VCT and support for disclosure
- HIV infected people on treatment should be advised about prevention benefits
- Treatment for HIV-positive partners with ≥ 350 CD4 cells in a serodiscordant relationship to prevent HIV transmission

… “there is no reason to believe ART will not prevent transmission in MSM couples”
Clinton speech November 8, 2011 at US National Institutes of Health
HPTN 071 (PopART)

- Effect of combination prevention interventions anchored in universal ART on community HIV incidence
  - Home and clinic-based testing
  - Linkage
  - ART
  - PMTCT
  - VMMC
HPTN 052 Recognition

U.S. Sponsors:
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• HPTN Leadership

AIDS Clinical Trials Group (ACTG):
• ACTG Leadership and Investigators

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