STATE OF THE NETWORK: HPTN – THE WAY FORWARD

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HPTN, Network PI
ICAP-Columbia University
From 3.5 to 2.3 Million

From 2.3 Million to 1.3 Million

From 550,000 to 260,000

9.7 Million Persons Initiated ART
Efficacious Prevention Interventions

Randomized, Controlled Intervention Trial of Male Circumcision for Reduction of HIV Infection Risk: The ANRS 1265 Trial

Effectiveness and Safety of Tenofovir Gel, an Antiretroviral Microbicide, for the Prevention of HIV Infection in Women

Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

Prevention of HIV-1 Infection with Early Antiretroviral Therapy
2.5 million new infections every year

The HIV Prevention Trials Network (HPTN) is committed to advancing HIV prevention through the use of integrated strategies, centered on the goal of reducing HIV incidence in populations at greatest risk for infection.
Select Network Achievements
HPTN 071 (PopART) Study

Purpose:
To determine the population effectiveness of universal testing and immediate ART initiation on HIV incidence

• Community-randomized study

• 21 communities (12 in Zambia, 9 in South Africa)

• Population: **1.2 million persons**
HPTN 071 (PopART) Intervention Package

• Annual home-based counseling and testing by Community HIV-care Providers (CHiPs)

• Information, active referral and support by CHiPs:
  – VMMC for HIV-uninfected men
  – PMTCT for HIV-infected women
  – Care for all HIV-infected individuals
  – Referral for sexual health and TB services
  – Condom provision
**Primary objective:** Measure the impact of PopART intervention on HIV incidence

- **Trial Design:**
  
  **3 arm cluster-randomised trial with 21 communities**
  
  (N ≈ 1.2 million total population)

  - **Arm A:**
    - Full PopART intervention
    - including
      - immediate ART irrespective of CD4 count

  - **Arm B:**
    - PopART intervention except
      - ART initiation according to current national guidelines*

  - **Arm C:**
    - Standard of care at current service provision levels
    - including
      - ART initiation according to current national guidelines

  - **21 communities in 3 arms**
    - 12 communities in Zambia
    - 9 communities in South Africa

- **Average population of ~50,000 in each cluster (~50% adults)**
- **Intervention delivered annually, door-to-door by field workers**
- **Incidence measured in Population Cohort (PC): (52,000 individuals)**
  - 2,500 adults in each cluster, followed up after 1, 2 and 3 years
All field activities commenced between January and March 2014

**Zambia**
- 37,775 households visited (~40%) and 59,820 adults have consented to participate in the intervention (through 30 April 2014)
  - 4531 (15%) enrolled in PC (through 11 June 2014)

**South Africa**
- 12,766 households visited (~23%) and 14,572 adults have consented to participate in the intervention (through 30 April 2014)
  - 5850 (26%) enrolled in PC (through 11 June 2014)
HPTN 065: Test Link to Care Plus Treat (TLC-Plus) Study

Purpose:

To evaluate the feasibility of an enhanced community-level HIV test, link-to-care plus treat strategy in the U.S.
HPTN 065 Interventions

- Social Mobilization
- Universal C&T in ED and inpatient wards

Expanded HIV Testing

- Financial incentives
- 37 testing sites

Linkage to Care

- Financial incentives
- 39 care sites

Viral Suppression

- Computer-based prevention intervention

Prevention for Positives

- Pre and post survey
  - Care providers
  - Patients

Provider and Patient Surveys
HPTN 065: Implementation Timeline

2010 2011 2012 2013 2014 2015

- Expanded Hospital Testing
- Social Mobilization
- Linkage-to-Care and Viral Suppression
- Prevention for Positives

- Provider Surveys
- Patient Surveys (part of PfP)
Intersection Between Surveillance and Research

Partnership with CDC and Departments of Health

- HIV Surveillance data used to assess outcome of site randomized financial incentive components (linkage and viral suppression)

- DOH data from New York, Washington DC, Chicago, Miami, Philadelphia, and Houston

- Strengthening HIV surveillance data through novel public health research
HPTN 068:
Effects of Cash Transfer for the Prevention of HIV in Young South African Women
Does providing cash transfers to young women and their household, conditional on school attendance, reduce structural barriers to education and thereby reduce young women’s risk of acquiring HIV?
HPTN 068

• A Phase III individually randomized design

• Girls (13-20 years) 8-11 grade in South Africa

• A total of 2,536 young women were randomized (enrollment complete)
PrEP Studies

- **HPTN 066**: PK for intermittent PrEP (FTC/TDF) (completed)
- **HPTN 067**: PK and behavioral study of alternative FTC/TDF dosage schedules including event-driven
  - N= 540 participants (360 MSM/TGW) and 180 women
  - Total of 622 individuals enrolled (US (Harlem), Bangkok and Capetown)
  - Follow-up to be completed by December 2014
- **HPTN 069**: Maraviroc (CCR5 inhibitor) (n-540)
  - oral alternative to FTC/TDF
  - 400 MSM and 200 women
  - 406 MSM (enrollment completed), 121 women enrolled
- **HPTN 073**: Uptake of FTC/TDF by black MSM
  - 225 black MSM
  - 75% enrolled
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<td>1252</td>
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<td>3860</td>
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<td>HIV negative</td>
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<td><strong>Total</strong></td>
<td>20,588</td>
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2013-2014 Publications

- 64 Published Manuscripts
  - JAIDS Supplement
  - HPTN 061 – 9 Manuscripts
HPTN Laboratory Center

- Comprehensive PK/PD Analyses
- Drug metabolism/pharmacogenetics
- Analysis of ARV use
- Cross-sectional HIV incidence estimation
- Phylogenetic analyses
Insights from HPTN Laboratory Center


- Provided key data for modeling/simulation studies that can help achieve optimal tissue concentrations of phosphorylated TFV

- Provided new insights into the metabolism of ARV drugs and the potential for intra-individual variation in drug activation and clearance

- Multi ARV screening assay provides a direct, biomedical assessment of ARV drug use in study communities, which can significantly impact study outcomes.
  - When combined with HIV drug resistance testing, this assay provides novel information about the risk of resistance including transmitted adherence

- Robust methods for cross-sectional HIV incidence estimation for clad B, C/A, which may be used for estimating HIV incidence in RCT

- Phylogenetic analyses provided information needed to characterize study cohorts, to understand the dynamics of HIV transmission in study populations (HPTN 052, MSM in US)
HPTN-SDMC: Data collection methods

Ongoing standards
- DataFax: Paper based data collection with electronic submission and recognition
- LDMS: Specimen management

Newer technologies
- DataStat Illume: Web-based ACASI and CASI data collection
- Surveillance data collaboration with CDC and DoH: Web Portal upload
- Distributed data collection for aggregated data about financial incentives
- Anonymous provider surveys
- Web tools for data entry using LabKey
- Sexual network: Interview administered web-based data collection
- WisePill: Adherence system data over cell networks
- EDC in households using tablet computers
HPTN SDMC: Mathematical Modelling to support HPTN research activities

Modelling to support HPTN studies

→ Planning vanguard studies
→ Post Vanguard : Go/No Go
→ Go: Before trial - Design
   After trial    - Interpretation of results
                  - Generalization of results
                  - Cost-effectiveness analysis

Improve & extend the application of models to prevention science

– Provide modelling support to HPTN teams
– Exchange of modelling ideas
Community Engagement

- Foster community partnership at all levels
- Enable innovations to enhance study performance
- Promote national-level engagement of focus communities (Black Caucus, stakeholder consultations, webinars)
- Develop and disseminate education materials (fact sheets, social media, presentations, guides)

Twitter.com/HIVptn
Facebook.com/HIVptn
website: www.hptn.org
Ethical Considerations in HPTN Studies

- **Risk Mitigation for MSM in Africa and PWID**
  - HPTN 075 (MSM in Africa)
  - HPTN 074 (TasP in PWID in Eastern Europe and Asia)

- **Standard of Care for PWID**
  - HPTN 074 (TasP in PWID in Eastern Europe and Asia)
  - HPTN 058 (PWID)

- **Comparator Arm for PrEP Studies (Standard of Care for Prevention)**
  - HPTN 076 (TMC278 LA)
  - HPTN 077 (GSK 744)

- **Financial Incentives for HIV Prevention**
  - HPTN 068 (School Girls in SA)
  - HPTN 065 (Linkage & VS US)

- **Informed Consent in Site and Community-Randomized Studies**
  - HPTN 065 (TLC-Plus)
  - HPTN 071 (PopART)

- **Informed consent in minors**
  - HPTN 068 (School Girls in SA)
HPTN Scholars

- Goal: to develop the next generation of HIV prevention scientists from underrepresented racial/ethnic communities
- Celebrating completion of the 4th cohort

Dr. DeMarc Hickson  
Dr. Larissa Jennings  
Dr. Malika Roman Isler  
Dr. Grace (Chela) Hall  
Dr. Tandrea Carter  
Dr. Jennifer Stewart  
Dr. Brooke Montgomery
# HPTN Scholars

## Welcoming our 5th Cohort

<table>
<thead>
<tr>
<th>Scholar</th>
<th>Mentor(s)</th>
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<tbody>
<tr>
<td>Dr. Laramie Smith</td>
<td>Dr. Carl Latkin, Dr. Steffanie Strathdee</td>
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<tr>
<td>Dr. Nicole Salazar-Austin</td>
<td>Dr. Tom Coates, Dr. David Celentano</td>
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<tr>
<td>Dr. Tiarney Ritchwood</td>
<td>Dr. Audrey Pettifor</td>
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<td>HPTN 062, HPTN 068</td>
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<td>Dr. Bisola Ojikutu</td>
<td>Dr. Steven Safren</td>
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I. Integrated Strategy Studies

Biomedical

Structural

Behavioral
INTEGRATED STRATEGIES FOR HIV PREVENTION

Behavioral

Structural

Biomedical

Integrated Strategy Trials

Reduce HIV incidence

PUBLIC HEALTH IMPACT
Why are Young Women In Southern Africa at Particularly High Risk for HIV?

- **Individual**: Young age, low perceived risk
- **Partner**: Older, unknown HIV status, unmarried or living together
- **Biological**: High pregnancy rates with increased risk of HIV during pregnancy; high STI prevalence
- **Structural**: Gender inequality, gender-based violence, poverty associated with transactional sex
Effectiveness and Adherence to TNF-based PrEP Regimens

Abdool Karim, S, Personal Communications

(Effectiveness vs. Percentage of participants’ samples with detectable drug levels
(Calculations based on analyses involving a subset of total trial participants)
Pearson correlation = 0.86, p=0.003)
Proposed Integrated Strategy
Research Agenda

Priority Populations

- MSM in the Americas
- Young women in Southern Africa
- Persons who inject drugs (PWID) in Eastern Europe and Asia
Global HIV prevalence of HIV in MSM compared with regional adult prevalence

2012 HSRC National HIV Survey
South Africa

• HIV incidence was 4.5% in black African females 20-34yrs

• Worrisome trends:
  – Condom use went down,
  – Knowledge decreased (only 26%),
  – low risk perception (76% at low risk)

Persons Who Inject Drugs

Lancet 2010 376: 551-563
Vanguard to Integrated Strategy Studies

Vanguard Study

• Recruit and retain population
• Uptake of intervention(s)
• Adherence, persistence

Go/no Go Decision

Integrated strategy Phase III Study

Findings from other studies
Modelling research results
Vanguard Studies (in Progress)

Vanguard Study
HPTN 074 – PWID
HPTN 075 – MSM SSA

Go/ No Go

Phase 3 Efficacy Study
HPTN 075 - MSM in SSA
A Vanguard Study

Observational study
400 MSM in 4 sites in SSA
12 months of follow-up
Outcomes
- Recruitment and retention
- Social harms
- STI and HIV incidence
- Risk behavior

Study Sites
- Kenya
- Malawi
- South Africa (2)
HPTN 074 – ART in PWID

Purpose of Vanguard Study

- Determine HIV incidence
- Recruit and retain index and partners
- Assess uptake and retention of ART for HIV-infected index
- Engage and retain in substance use treatment
- Characterize injection networks
- Assess social harms/benefits
- Measure phylogenetically-linked HIV transmission
**HPTN 074 Study – ART PWID**

**Design**

- **500 HIV-infected PWID (index patients)**
- Recruitment of at least one network injection partner
- Randomization: 1:3 ratio

**Integrative Strategy**
- Psychosocial Support
- Peer Navigation
- ART at any CD4 count

**Standard of Care**
- ART as per National Guidelines

**Outcomes**
- HIV incidence
- Recruitment and Retention of Index and Partners

**Sites**
- Indonesia
- Ukraine
- Vietnam

*Follow-up for all index participants is 12-24 months*
Vanguard Studies (in Development)

Vanguard Studies
HPTN 078 – HIV+ MSM
HPTN 079 – VMMC HIV- MSM
HPTN 080 – SexPro (PrEP)

Go/ No Go

Phase 3 Efficacy Study
Way Forward
II. Pre-exposure Prophylaxis (PrEP)
Pre-exposure Prophylaxis (PrEP)

Two Goals

1. Optimize effectiveness of emtricitabine/tenofovir disoproxil fumarate (FTC/TDF)

2. Develop novel agents/regimens for PrEP
Integrated Strategies
PrEP

HIV-UNINFECTED PERSONS

Behavioral
Maximize ARV Effectiveness
PREP
Structural
Biomedical

Better use of Current PrEP Drugs
Evaluate new PrEP Drugs
Conclusions

• Great progress has been achieved in confronting the global HIV epidemic
  – Several prevention methods have been shown to work
• Nonetheless, large number of new HIV infections continue to occur
• Progress achieved in multiple studies focused on diverse populations
• Future prevention efforts will require:
  – Continuing to seek new methods for prevention
  – Use of integrated strategies that combine various interventions
• Engaging communities and supporting new generation of scientists is key to achieve this ambitious HIV prevention agenda
Acknowledgements

• NIH Institutes (NIAID, NIMH, NIDA)

• Office of AIDS Coordinator (OGAC), Gates Foundation

• HPTN Scientific Committees, Working Groups, Executive Committee and Scientific Advisory Group

• Study participants and participating communities

• HPTN investigators, staff and community members

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