HPTN
State of the Network

Accomplishments and Way Forward

Wafaa El-Sadr, MD, MPH, MPA
Remarkable progress achieved in HIV prevention

- Yet, HIV transmission remains a challenge with alarming rates in specific populations and regions

These realities inspire the HPTN research agenda

**HPTN Mission**

Advance HIV prevention through the use of integrated strategies, centered on the goal of reducing HIV incidence in populations at greatest risk for infection

**Prevention at the Crossroads**

- New HIV infections reduced from 3.5 to 2.3 Million
  - 33% decrease in new HIV infections since 2001
  - 29% decrease in AIDS-related deaths (adults and children) since 2005
  - 52% decrease in new HIV infections in children since 2001
  - 40-fold increase in access to antiretroviral therapy 2002–2012

UNAIDS 2014
The Year in Review

- Four studies completed
- Seven ongoing studies… including the largest HIV prevention study to date!
  - Four new studies initiated
- Four studies in development
- More than 106,000 participants in recent studies
  - more than 43,000 participants in current studies
- Robust engagement of communities
- Continued success by our scholars
2014-2015 Publications

67 Publications

Presentations

• IAS 2015 – 14 abstracts accepted including 8 late breakers
• CROI 2015 – 7
• R4P 2014 – 8
• IAS 2014 – 8
• CROI 2014 - 4

HIV and Women Who Inject Drugs:
HPTN SUSC Chair and Co-chairs:
Nabila El-Bassel and Steffanie Strathdee
Studies Completed in Past Year

- HPTN 065 (Feasibility of Test and Treat in US)
- HPTN 052 (ART for prevention in discordant couples)
- HPTN 068 (Financial incentives, conditional on school attendance, in young women SA)
- HPTN 067 (Adherence, PK FTC/TDF for PrEP)
HPTN 065

Expanded HIV Testing
- Social Mobilization
- Universal HIV testing in hospitals (ED & IP)

Linkage to Care
- Financial Incentives
  - $25
  - $100

Viral Suppression
- Financial Incentives
  - $70

Prevention for Positives

Provider and Patient Surveys
- Pre and post survey
  - Providers
  - Patients

Financial Incentives

CROI 2015
HPTN 052, Interim Results, 2011

96% decrease in HIV transmission

Total HIV-1 Transmission Events: 39

Linked Transmissions: 28
- Immediate Arm: 1
- Delayed Arm: 27

Unlinked Transmissions: 11

p < 0.001

Final Analysis

NEJM, August 2011
Effects of Cash Transfer For the Prevention of HIV in Young South African Women

**Enrollment**

<table>
<thead>
<tr>
<th></th>
<th>2,537</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>13-20 yrs</td>
</tr>
</tbody>
</table>

**Intervention**

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,263</td>
<td>1,274</td>
</tr>
<tr>
<td>Cash transfer conditional on school attendance</td>
<td>No cash</td>
</tr>
</tbody>
</table>

Interested women who previously exited the study are being asked to return to clinic through August 2015 to determine durability of the intervention.

**Primary outcome:** Primary HIV Incidence
HPTN 067 (ADAPT)

Randomized, Open-Label, PK and Behavioral Study of the Use of Daily and Intermittent Oral FTC/TDF for PrEP

Regimens
- Daily (D) Time Driven:
- Twice weekly and post-intercourse boost (T)
- Event-driven: Before and after sex (E)

Primary objective:
To compare daily versus non-daily FTC/TDF:
- coverage of sex events
- Number of pills for coverage
- side effects

Three Sites | Randomized | Results
--- | --- | ---
HIV-uninfected at risk MSM/TGW Cape Town, South Africa | 179 | IAS 2015
Young women in Africa will take oral PrEP
HIV-uninfected at risk MSM/TGW Bangkok, Thailand | 178 | IAS 2015
HIV-uninfected at risk MSM/TGW NYC (Harlem), USA | 179 | IAS 2015
Scientific Agenda
Ongoing and Planned Studies

Pre-Exposure Prophylaxis (PrEP)
Integrated Strategies for Prevention
Scientific Agenda
Ongoing and Planned Studies

Pre-Exposure Prophylaxis (PrEP)

Integrated Strategies for Prevention
Pre-Exposure Prophylaxis (PrEP)
Oral Maraviroc
Injectable rilpivirine
Injectable cabotegravir
VRC01 monoclonal antibody
HPTN 069 – Phase 2 Safety and Tolerability of Maraviroc for PrEP

**Study Design**
- Phase 2
- Double-blind
- Randomized

**Location**
- 13 sites – U.S.

<table>
<thead>
<tr>
<th>Arm</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MVC alone</td>
</tr>
<tr>
<td>2</td>
<td>MVC + FTC</td>
</tr>
<tr>
<td>3</td>
<td>MVC + TDF</td>
</tr>
<tr>
<td>4</td>
<td>FTC + TDF</td>
</tr>
</tbody>
</table>

**Primary Outcome:** Safety, Tolerability of four regimens used as PrEP

**Study Status**
- Follow-up ends in November 2015
- Target abstract for IAS 2016
- Follow-up completed April 2015
- Target abstract for CROI 2016
A Phase II Study of Safety and Acceptability of Injectable Rilpivirine (TMC278 LA) for PrEP

132 HIV-uninfected, ages 18-45

WEEKS

<table>
<thead>
<tr>
<th>ARM 1</th>
<th>Daily Oral TMC278</th>
<th>Six doses of injections of Rilpivirine every 8 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 88</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ARM 2</th>
<th>Daily oral placebo</th>
<th>Six doses of injections of placebo every 8 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 44</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Follow-up phase (tail phase)

Primary outcome: Safety of rilpivirine in women in sub-Saharan Africa and the U.S.

- Activation in March 2015
- 31 Enrolled to Date (25%)
  - Bronx, NY
  - Newark, NJ
  - Harare, Zimbabwe
  - Cape Town, SA
A Phase IIa Study of Safety, Tolerability and PK of Injectable Cabotegravir (744 LA) in HIV-uninfected Men and Women

**ARM 1**
- N = 132
- Daily Oral cabotegravir
- Three injections of cabotegravir every 12 weeks

**ARM 2**
- N = 44
- Daily Oral Placebo
- Three injections of placebo every 12 weeks

Follow-up Phase (Tail Phase)

**US Sites**
- Los Angeles, California
- San Francisco, California
- Washington, DC
- Chapel Hill, North Carolina

**International Sites**
- Soweto, South Africa
- Durban, South Africa
- Lilongwe, Malawi
- Rio de Janeiro, Brazil

**Primary outcome**: Safety and tolerability of injectable cabotegravir LA in HIV-uninfected men and women

**176** HIV-uninfected, Ages 18-65

**WEEKS**
- 4
- 41
- 81

30 enrolled to date (17%), 14 men and 12 women
HPTN 083 Inj Cabotegravir (in development)

A Phase 2b/3 Double Blind Efficacy Study Of Injectable Cabotegravir Compared to Daily Oral TDF/FTC, For PrEP in HIV-Uninfected Men and TGW

<table>
<thead>
<tr>
<th>Study Size</th>
<th>N=4500</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Duration</td>
<td>3-5 years</td>
</tr>
<tr>
<td>Location</td>
<td>North and South America and Asia</td>
</tr>
</tbody>
</table>

**Arm A**

**Step 1**
Daily oral CAB and oral TDF/FTC placebo

**Step 2**
Injectable CAB every 12 weeks and daily oral placebo

**Step 3**
Open-label daily oral TDF/FTC to cover the PK tail, for up to 48 weeks

**Arm B**

**Step 1**
Daily oral TDF/FTC and oral CAB placebo

**Step 2**
Daily oral TDF/FTC and injectable placebo every 12 weeks

**Step 3**
Transition to locally-available HIV prevention services

**Primary Outcome:**
HIV incidence
Enrolled participants

- 2400 MSM and TG + 1500 women
- 18 to 50 years of age

Study duration

- 92 weeks
- (infusions given through week 72)

A phase 2b study to evaluate the safety and efficacy of VRC01 broadly neutralizing monoclonal antibody in reducing acquisition of HIV-1 infection

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Total</th>
<th>Infusions every 8 weeks through Week 72</th>
</tr>
</thead>
<tbody>
<tr>
<td>VRC01 10 mg/kg</td>
<td>2600</td>
<td>10 infusions/participant</td>
</tr>
<tr>
<td>VRC01 30 mg/kg</td>
<td>1300</td>
<td></td>
</tr>
<tr>
<td>Control*</td>
<td>1300</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>3900</td>
<td></td>
</tr>
</tbody>
</table>

*Access to PrEP where possible

Primary outcome: HIV incidence, safety and tolerability
Integrated Strategies for HIV Prevention

1- Oral PrEP (FTC/TDF)
2- ART for Prevention
Integrated Strategies

1- Oral PrEP (FTC/TDF)
2- ART for Prevention
FTC/TDF for PrEP

- Potent
- Safe
- Easy to take
- Demonstrated efficacy when adherent

AVAC Report (2013)
Black MSM in the US
HPTN 061

• Overall HIV incidence 3% (95% CI 2-4.4)
• HIV incidence in men <30 yrs: 5.9%
  (95% CI 3.6-9.1%)
• Younger men: more STIs, more barriers to health care
Pre-Exposure Prophylaxis (PrEP) Initiation and Adherence Among Black MSM in the US

**Enrollment**
- 226

**Population**
- BMSM/HIV-

**Study Duration:** 12 M Enrollment 12 M Follow-up

**Primary Outcomes:**
- Initiation of daily PrEP use by socio-demographics including age, education, and risk practices
- PrEP adherence via self report (ACASI) and ARV detection

**HIV negative BMSM**

Provide PrEP Daily Oral TDF/FTC + Client Centered Care Coordination (C4)
Study Update

Study Start: Aug 2013

Fully Enrolled: Sept 2014

Follow-up Completion: Sept 2015

Washington, DC
Los Angeles, CA
Raleigh, NC

41% of participants ≤ 25
78% initiated PrEP
92% retention
Adolescents and young women in Sub Saharan Africa

- Alarmingly high HIV incidence: 6% annually FemPrEP/VOICE
- Limited efficacy of behavioral interventions to change behavior or reduce STI/HIV incidence
- Young women may be less likely to realize benefits of ART for prevention & VMMC
  - Challenges in getting men to test, link to and stay in care
  - Slow VMMC scale-up in some countries; lower uptake in men in their 20s and 30s
- HPTN 067 showed high adherence with oral open label FTC/TDF PrEP in SA

Adapted, Celum 2015
**Target Enrollment**

- Uninfected women, 16-25 yrs, southern Africa
- 400 women who accept PrEP at enrollment
- Up to 200 women who decline PrEP at enrollment

**Follow-up duration:** 12 months

**Evaluation of daily oral PrEP for young African women:**

- **Enroll**
- **Accept**
  - Provide PrEP, adherence support, blood levels & SOC (400 women)
- **Decline**
  - SOC and offer PrEP (up to 200 women)

**Primary outcome:**
PrEP initiation, adherence, acceptability, and continuation

**Qualitative research in subset of participants**
Integrated Strategies

1- Oral PrEP (FTC/TDF)
2- ART for Prevention
Global ART coverage

37%

Adults and children

Continuum of HIV Care SSA

UNAIDS 2014
Community Level
ART initiation according to current national guidelines

PopART intervention except
3 arm cluster-randomised trial with 21 communities

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

Study Communities
• 21 communities
• Average 50,000 persons/community
• Total population: about 1.2 Million

Primary Outcome: HIV Incidence Measured in Population Cohort (PC)
• 2,500 randomly selected adults from each community cluster (about 52,000
• Followed at 12, 24 and 36 months
All field activities commenced between January and March 2014

Zambia
- 96,847 households visited
- 244,502 adults consented for intervention
- 19,756 (66%) enrolled in PC0

South Africa
- 55,853 households visited
- 110,652 adults consented for intervention
- 18,626 (83%) enrolled in PC0
People Who Inject Drugs (PWID)
<table>
<thead>
<tr>
<th>Intervention</th>
<th>Standard of Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>125 HIV +</td>
<td>375 HIV +</td>
</tr>
<tr>
<td>188 HIV – Partners</td>
<td>563 HIV – Partners</td>
</tr>
</tbody>
</table>

15 Months Recruitment
12 Months Follow-Up

A study comparing an integrated intervention including supported ART to standard of care for PWID

Ukraine
Vietnam
Indonesia
Primary Objective: Assess HIV incidence, recruitment, retention, and feasibility and barriers of the intervention
MSM in the US
Continuum of HIV Care--US

Of all with HIV infection, 850,000 individuals do not have suppressed HIV RNA (72%)

MMWR (60), 2011
A Study to Enhance, Recruit, Link to Care and Treat for HIV-Infected MSM in the US

**Screened population** | **Enrolled participants**
---|---
2700 | 356
MSM >= 16 yo | MSM/ HIV+

**Study Duration:**
12 M Enrollment
24 M Follow-up

**Deep-Chain Respondent Driven Sampling**

**Primary objectives:** Recruitment feasibility and viral suppression

**Intervention** (n = 178)

**Case Manager Intervention Package**

**Control** (n = 178)

**SOC for Linkage and Treatment**
HIV Care Continuum and the Case Manager Intervention

Based on data from: http://www.cdc.gov/hiv/pdf/research_mmp_stagesofcare.pdf
New Populations at Risk

- MSM in SSA (HPTN 075)

Exploration

- Sex workers
- Non-injection substance users
- Transgender people
Feasibility of HIV Prevention Cohort Studies Among MSM in Sub-Saharan Africa

Observational study:

400 MSM in 4 Sites
- Men 18-44 years living in Sub-Saharan Africa who report anal sex with a man in the past 3 months

12 Months of Follow-Up
- 5 study visits with structured HIV behavioral assessments, medical examinations, and collection of biological samples

Primary Outcome:
Recruitment and retention of cohort
## Prevalence of Transactional Sex in HPTN Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Study type</th>
<th>Number and percent reported exchanging sex for money/resources</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPTN 067 (n=537)</td>
<td>PrEP</td>
<td>81, 15%</td>
</tr>
<tr>
<td>HPTN 068 (n=2533)</td>
<td>Incentives</td>
<td>97, 4%</td>
</tr>
<tr>
<td>HPTN 069 (n=593)</td>
<td>PrEP</td>
<td>39, 7%</td>
</tr>
<tr>
<td>HPTN 071 (n=38,382)</td>
<td>Integrated</td>
<td>5275, 14%</td>
</tr>
<tr>
<td>HPTN 073 (n=226)</td>
<td>PrEP</td>
<td>28, 12%</td>
</tr>
</tbody>
</table>
HIV and Sex Workers

• Female sex workers make up a sizeable minority of the adult female population globally
  – Cities in Sub Saharan Africa - 0.7% - 4.3%
  – If include transactional sex more broadly up to 9.4%

• Female sex workers bear a disproportionate burden of HIV
  – 13.5 times more likely to be HIV positive

• Modelling suggests population attributable fraction due to FSW in SSA will increase over time and interventions which impact HIV incidence in FSWs in SSA will also impact incidence more broadly
# Injection and Non-injection Substance Use (cocaine) in HPTN Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>Injection drug use</th>
<th>Cocaine (powder + crack)</th>
<th>All non-injection (not including MJ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPTN067</td>
<td>PrEP</td>
<td>16 3%</td>
<td>132 15%</td>
<td>258 29%</td>
</tr>
<tr>
<td>HPTN069</td>
<td>PrEP</td>
<td>34 6%</td>
<td>124 21%</td>
<td>302 51%</td>
</tr>
<tr>
<td>HPTN073</td>
<td>PrEP</td>
<td>2 1%</td>
<td>41 18%</td>
<td>77 34%</td>
</tr>
</tbody>
</table>
Non-Injection Substance Use

- Most substance use is non-injection and is common in at risk groups (Youth, MSM/MSMW, TG, SW)

- Non-injection substance use is linked to condomless sex in at-risk groups

- Non-injection substance use associated with altered biology that may increase risk of HIV acquisition or transmission
HIV and Transgender People

• High and disproportionate burden of HIV among transgender women (TGW):
  – Pooled global HIV prevalence 19.1% (95% CI 17.4-20.7)
  – 48.8 times the odds of the general population (95% CI 31.2-76.3)

• Current interventions designed for MSM fail to effectively reach TGW or reduce HIV vulnerability.
  – TGW do not enroll in studies or interventions designed for MSM in large enough numbers for substantive analysis
  – Low serum concentrations of TDF among TGW on hormones
Community Engagement

- Increase scientific literacy through capacity building workshops
- Apply lessons learned and best practices to overcome historic mistrust and improve study implementation
- Foster community and research partnerships through strategic local and national engagement
- Use of social media venues for information dissemination
HPTN Scholars Program

Goal: To develop the next generation of HIV prevention scientists from underrepresented racial/ethnic communities

To date: 21 scholars completed program
20 mentors engaged
Utilize HPTN data to develop analytic skills, conduct reviews, presentations/publications
K awards, R03, Faculty positions, Presentations, Publications

International Scholar Program!
HPTN Scholars

Celebrating the 5th cohort

Dr. Bisola Ojikutu
Dr. Tiarney Ritchwood
Dr. Nicole Salazar-Austin
Dr. Laramie Smith

Welcoming the 6th Cohort

Dr. Brandon Brown
Dr. Dustin Duncan
Dr. Mandy Hill
Dr. Florence Momplaisir
Dr. Tonia Poteat

Dr. Tom Coates
Drs. Ken Mayer & Steve Safren
Dr. Carl Latkin
Drs. Carl Latkin & David Metzger
Dr. David Celentano
Conclusions

• HPTN is conducting and planning prevention studies within a cohesive framework that aims at both innovation and impact

• HPTN research portfolio is diverse focusing on priority populations and settings

• Developing the next generation of prevention researchers is a key priority

• Engaging communities from day one in every aspect of the research endeavor is a pre-requisite for success
Acknowledgements

- HPTN Scientific Committees, Working Groups, Executive Committee and Scientific Advisory Group
- Investigators, staff and community representatives
- Study participants and participating communities

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