Mechanisms and Ways to generate research concepts and address research gaps

Wafaa El-Sadr, MD, MPH
HPTN South America Regional Meeting
March 26, 2018
Lima, Peru
Outline of Presentation

• HPTN research priorities
• Identifying research gaps
• Answering the key questions
  – Vanguard studies
  – Ancillary studies
• Concept/protocol development process
• Way forward
HPTN Mission

To advance HIV prevention through the use of integrated strategies, centered on reducing HIV incidence in populations at greatest risk for infection.
Focus of the Research

• To identify new PrEP agents/regimens

• To design/implement integrated strategy studies
HPTN Research Focus

POPULATION SPECIFIC
• Young Women
• MSM
• PWID
• High Prevalence Community

HIV-INFECTED
- Behavioral
- Structural
- Biomedical
- Maximize ART Effectiveness

HIV-UNINFECTED
- Behavioral
- Structural
- Biomedical
- Maximize ART Effectiveness

Integrated Strategy Study

Reduce HIV incidence

PUBLIC HEALTH IMPACT

New PrEP Agents

Vanguard Study

HIV-INFECTED HIV-UNINFECTED
van·guard: noun
A group of people leading the way in new developments or ideas
• a position at the forefront of new ideas
• foremost part of an advancing army or naval force

Foremost study that aim to be informative and positions HPTN for larger phase III studies or for incorporation of approach into other studies

Merriam Webster Dictionary
What Vanguard Studies Can Contribute?

- How to find the population of interest?
- Can the target population be recruited and retained in research studies?
- Will the intervention(s) be feasible and acceptable?
- Can a combination prevention strategy be successfully constructed and delivered?
- What is the HIV incidence in a specific population?
Optimizing PrEP Use

MSM in the US
HPTN 073
Vanguard Questions:

• What is the feasibility of recruitment and retention of cohort of HIV-negative Black MSM?

• What is the feasibility, acceptability and effectiveness of Coordinated Clinical Care Coordination (C4) intervention to enhance uptake and adherence with oral daily PrEP?
HPTN 073 Findings

- Recruitment and retention of Black MSM in US is feasible
- Implementation of C4 feasible and acceptable
- C4 associated with uptake and adherence with oral PrEP
- Substantial HIV incidence among participants
- Engagement of HPTN Black Caucus advantageous in design and implementation of the study

8 Conference Oral and Poster Presentations
Manuscript of primary results close to submission
Optimizing ART for Prevention

MSM in the US
What is the feasibility of recruitment of HIV-positive MSM with unsuppressed viral load using respondent-driven sampling (RDS) (and other methods)?

What is the feasibility of retention of cohort of HIV-positive MSM?

What is the feasibility, acceptability and effectiveness of an enhanced case management strategy in achieving viral load suppression?
HPTN 078
Enhancing Recruitment, Linkage to Care and Treatment for HIV-Infected Men Who Have Sex with Men (MSM) in the United States

Study Design

- **Screened population**
  - 2700
  - MSM >= 16 yo
  - HIV+, Unsuppressed

- **Enrolled participants**
  - 356
  - MSM
  - HIV+, Unsuppressed

Study Duration: 24 M Follow-up

**Deep-Chain Respondent Driven Sampling (DC-RDS), and other methods**

**Enhanced Case Manager Intervention**
(n = 178)

**SOC for Linkage and Treatment**
(n = 178)

**Individual Randomization**

**Study Design**

- Enhanced Case Manager Intervention
- Control
- SOC for Linkage and Treatment
- Deep-Chain Respondent Driven Sampling (DC-RDS), and other methods
- Individual Randomization
# HPTN 078 Status

<table>
<thead>
<tr>
<th>Location</th>
<th>Enrollment Target</th>
<th>Total Enrolled</th>
<th>Percent Enrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atlanta</td>
<td>89</td>
<td>48</td>
<td>54%</td>
</tr>
<tr>
<td>Baltimore</td>
<td>89</td>
<td>35</td>
<td>39%</td>
</tr>
<tr>
<td>Birmingham</td>
<td>89</td>
<td>34</td>
<td>38%</td>
</tr>
<tr>
<td>Boston</td>
<td>89</td>
<td>27</td>
<td>30%</td>
</tr>
<tr>
<td>Overall</td>
<td>356</td>
<td>144</td>
<td>40%</td>
</tr>
</tbody>
</table>

Closed to Enrollment
Randomized Cohort in Follow-up
Feasibility of Recruitment and Retention of MSM from Sub Saharan Africa
HPTN 075: Vanguard Questions

• What is the feasibility of recruiting and retaining a multi-country cohort of MSM from SSA?
• Can this be accomplished safely?
• What are characteristics of the MSM that need be taken into account in the design and implementation of interventions for this population?
• What is the HIV incidence among MSM in SSA?
HPTN 075: Recruitment

• Extensive preparation of sites for conduct of the study with tailored risk mitigation strategies

• Recruitment strategies varied by site, based on:
  – Input from CAB and MSM community informants
  – Earlier experiences
  – Informal networks, a common approach
## Screening, Enrollment, Study Completion

<table>
<thead>
<tr>
<th>Category</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screened</td>
<td>624</td>
</tr>
<tr>
<td>Ineligible:</td>
<td>223/624 = 35.7%</td>
</tr>
<tr>
<td>Enrolled:</td>
<td>401/624 = 64.3%</td>
</tr>
<tr>
<td>Deaths:</td>
<td>5/401 = 1.2%</td>
</tr>
<tr>
<td>Completed final visit (5):</td>
<td>368/396 = 92.9%</td>
</tr>
<tr>
<td>Missed visits (2, 3 and 4):</td>
<td>36*/1155 = 3.1%</td>
</tr>
</tbody>
</table>

* Consecutively missed visits of men who did not complete Visit 5 are excluded.
HPTN 075: Results to Date

- Recruiting and retention of MSM from sub-Saharan Africa is feasible
- With sufficient preparation such studies can be implemented without major social harms
- Implementing studies with this population enables acceptance by healthcare workers and CABs.
- HIV seroprevalence in this population is high

Stay tuned!
Optimizing Use of ART for Prevention
PWID in Eastern Europe and Southeast Asia
HPTN 074
Vanguard Questions

• What is the feasibility of recruiting HIV-positive PWID with unsuppressed viral load?
• What is the feasibility of recruitment of their HIV-negative injecting partners?
• What is the feasibility of retaining the cohort of index PWID and their partners?
• What is the feasibility, acceptability and effectiveness of integrated strategy to enhance ART and MAT uptake and adherence with ART?
• What is HIV incidence among partners of index PWID?
## Intervention Standard of Care

<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

Fully enrolled: 504 index participants, 810 network partners (total = 1314)
Primary Objective: Assess HIV incidence, recruitment, retention, and feasibility and barriers of the intervention.
HPTN 074: Results to Date

- 502 indexes and 806 partners enrolled with good retention
- Indexes in the intervention arm had better outcomes:
  - Higher ART use, viral suppression, MAT use
  - Lower mortality
- Partners of index participants in the intervention arm had lower mortality.
- All incident HIV infections among partners occurred in the SOC arm:
  - Intervention: incidence rate: 0.0/100 py; (CI 0.00, 1.7)
  - SOC: incidence rate: 1.0/100 py; (CI 0.41, 2.1)
  - Incidence rate difference: -1.0/100 p-y (CI -2.1, 1.1)
Optimizing PrEP Use

Young Women in Southern Africa
HPTN 082
Vanguard Questions

• What is the feasibility of recruitment and retention of young women from SSA?
• What is the feasibility, acceptability and effectiveness of integrated strategy for enhancing uptake and adherence with oral PrEP?
HPTN 082: Study Design

**PrEP = Daily oral FTC/TDF**

- Provide PrEP, enhanced adherence support, SOC (~200 women)
- Provide PrEP, standard adherence support, SOC (~200 women)

**SOC and offer PrEP (≤200 women)**

- Randomize PrEP Acceptors 1:1
- Accept
- Enroll
- Decline

**In-depth interviews about women’s decisions to use PrEP, adhere to PrEP, and acceptability. (~75 total, including acceptors and decliners)**

**Standard Adherence Support**
- CBT counseling
- SMS texting
- Adherence clubs

**Enhanced Adherence Support**
- CBT counseling
- SMS texting
- Adherence clubs
- Drug level feedback counseling
HPTN 082: Evaluation of daily oral PrEP as a primary prevention strategy for young African women

Study Population
- Uninfected women
  - Ages 16-25 yrs
- Johannesburg & Cape Town, South Africa
  - Harare, Zimbabwe

Target Enrollment
- 400 women who accept PrEP at enrollment
- ≤ 200 women who decline PrEP at enrollment

Primary objectives:
- Assess the proportion and characteristics of women who accept versus decline PrEP
- Assess PrEP adherence using drug levels in young women

Figure 1: PrEP uptake overall and by site

- Overall: 95%
- Harare: 97%
- Cape Town: 99%
- Johannesburg: 88%

PrEP not accepted
HPTN 082: Results to Date

- HPTN 082 had high uptake (95%) of PrEP
  - Despite reported low perceived risk of HIV
- Risk behavior is high (transactional sex (23% last months), never/rare/sometime (68%) condom use, high prevalence (39%) of curable STIs), indicating success in reaching young women at risk
- Half had symptoms of depression and reported intimate partner violence in the past year
- Low perception of risk for HIV, no/small risk (78%)
- High uptake of PrEP by the young women
  - Adherence data will indicate proportion with effective use & effect of drug level feedback
Vanguard Studies: What’s Next?

Knowledge gained:
- Methods to identify population of interest
- Feasibility of recruitment & retention of population
- Feasibility & acceptability of intervention(s)
- Adherence, persistence
- HIV incidence

Vanguard Studies

Go/ No Go

Other Information

HPTN Phase 3 Efficacy Study
HPTN: Ancillary Studies

- *De novo* research questions
- Can be layered into planned or ongoing studies (may be limited to a few sites)
  - Further understanding of issues of relevance to ongoing study
  - Obtain data to inform future research
- Analysis of data from completed studies (SDMC or LC)
Ancillary Study Form

HPTN Ancillary Investigation Checklist and Application

**Definition:**
Ancillary studies may involve collection of additional data and/or samples from study participants, or use of existing data and/or samples for analyses or laboratory assessments that are not directly related to the specific objectives of the relevant HPTN study as defined in the protocol document.

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Application Date:</td>
</tr>
<tr>
<td>2.</td>
<td>Title of the proposed study:</td>
</tr>
<tr>
<td>3.</td>
<td>Name and contact information for proposing HPTN Investigator(s) (include institutional affiliation, email, phone):</td>
</tr>
<tr>
<td>4.</td>
<td>Number and title of primary HPTN study to which the proposed study is linked:</td>
</tr>
<tr>
<td>5.</td>
<td>Name and contact information for non-HPTN Investigator(s) (include institutional affiliation)</td>
</tr>
<tr>
<td></td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

Note: All non-HPTN Investigators using biological specimens from HPTN

https://hptn.org/resources/manual-of-operations
Examples of Ancillary Studies

Validation of sexual and adherence behavior questions through cognitive testing
K. Rivet Amico, PhD
University of Michigan

HPTN 075 Participants and Injectable PrEP
Theo Sandfort

Assessing knowledge and willingness to use PrEP in general, the future acceptability of injectable PrEP, willingness to participate in injectable PrEP Trials and demonstration projects and factors associated with acceptability and willingness to use injectable PrEP.

ACCEPTABILITY AND USE OF PREP PRODUCTS AMONG WOMEN TOOL
Women at Risk Scientific Committee

Building Scientific Expertise in Substance Use-Related Risks for HIV Transmission in HPTN Protocols
Substance Use Scientific Committee
HPTN Science Generation Process

- Concept
- HPTN SC/LG
- HPTN or Non-HPTN Investigators
- EC Concept Review
- Final protocol sent to sites
- PSRC Review DAIDS Reviews
- Protocol Development
- Not Approved
- Approved
- EC Concept Review
Science Generation Process

Abbreviations:
- DAIDS Division of AIDS
- EC Executive Committee
- HPTN HIV Prevention Trials Network
- IRB Institutional Review Board
- PSRC Prevention Science Review Committee
- RAB Regulatory Affairs Branch
- SC Scientific Committee
- SRC Scientific Review Committee

HPTN Science Review Committee review & approval
- DAIDS Prevention Science Review Committee review & approval
- DAIDS regulatory review & approval
- DAIDS Medical or Program Officer review & approval
- DAIDS Regulatory Affairs Branch Chief sign-off on final version 1.0

Final protocol version to sites for preparation of site-specific consent forms and submission to IRBs/ECs
Way Forward

• Build on findings from vanguard studies and ancillary studies
  – HPTN 074 PWID and partners
  – HPTN 075 MSM in SSA
  – HPTN 073 & HPTN 078 MSM in US
  – HPTN 082 Adolescents/young women

• Transgender women
• Non-injection drug users (including alcohol)
• STI risk among study participants

Unique questions for South American sites
We welcome your ideas!!
Thank you
Gracias
Obrigada