



**HPTN**

HIV Prevention  
Trials Network

# **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

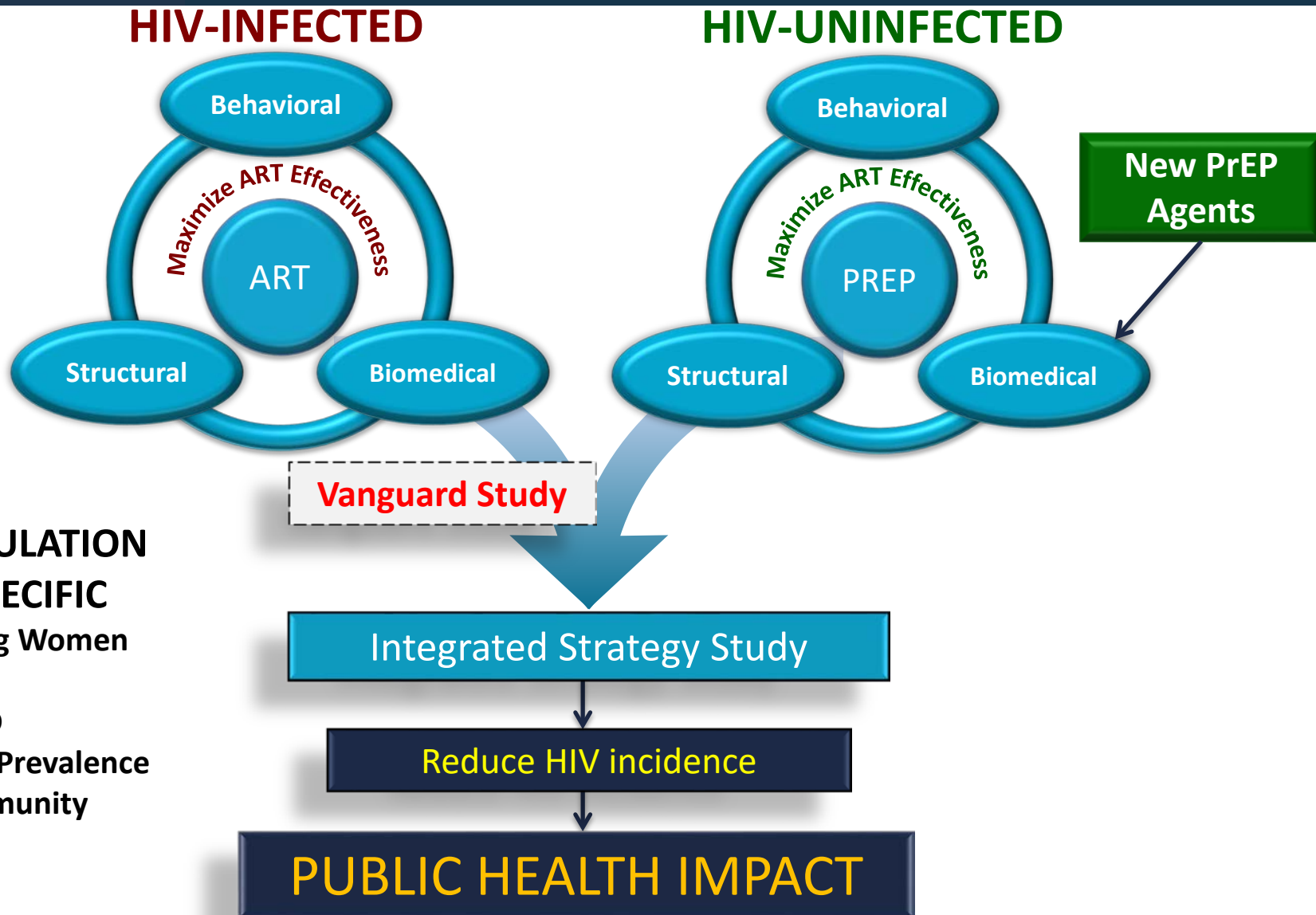
# HPTN Mission

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

# Vanguard: Definition

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

# 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



## HPTN 078

### Vanguard Questions:

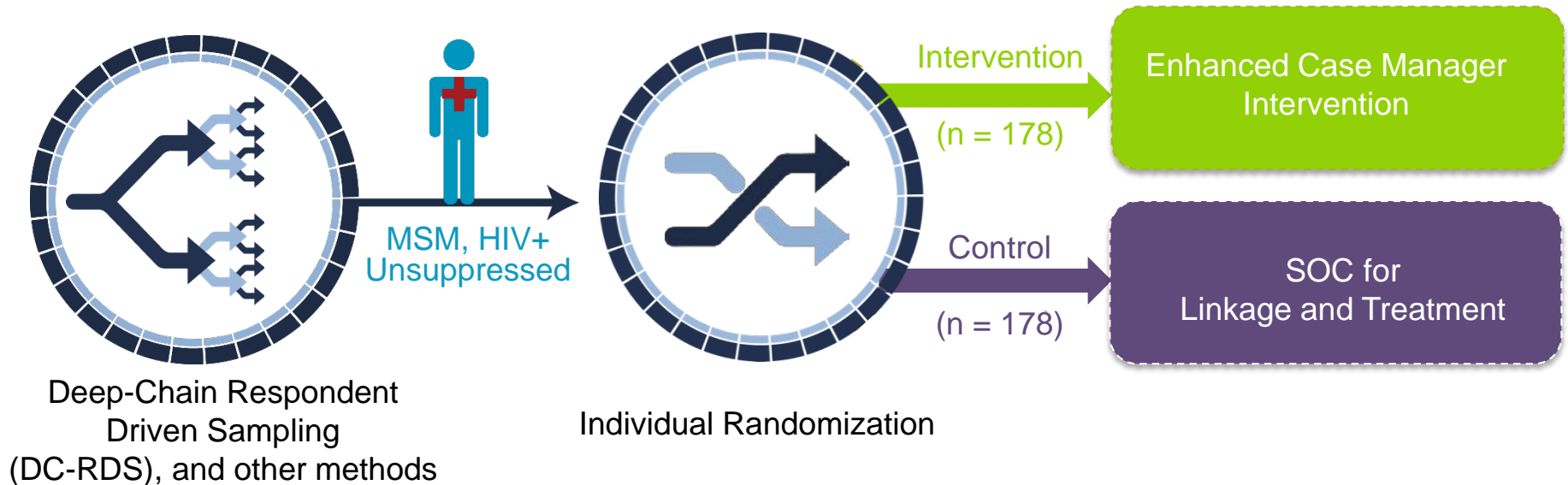
- What is the feasibility of recruitment of HIV-positive MSM with unsuppressed viral load using respondent-driven sampling (RDS) (and other methods)?
- What is the feasibility of retention of cohort of HIV-positive MSM?
- What is the feasibility, acceptability and effectiveness of an enhanced case management 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

Screened population	Enrolled participants
2700	356
MSM $\geq$ 16 yo	MSM HIV+, Unsuppressed
Study Duration: 24 M Follow-up	

## Study Design



## HPTN 078 Status

	Enrollment Target	Total Enrolled	Percent Enrolled
Atlanta	89	48	54%
Baltimore	89	35	39%
Birmingham	89	34	38%
Boston	89	27	30%
Overall	356	144	40%

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

Screened:	624
Ineligible:	$223/624 = 35.7\%$
Enrolled:	$401/624 = 64.3\%$
Deaths:	$5/401 = 1.2\%$
Completed final visit (5):	$368/396 = 92.9\%$
Missed visits (2, 3 and 4):	$36^*/1155 = 3.1\%$

\* 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!**



**AIDS 2018**

# 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?

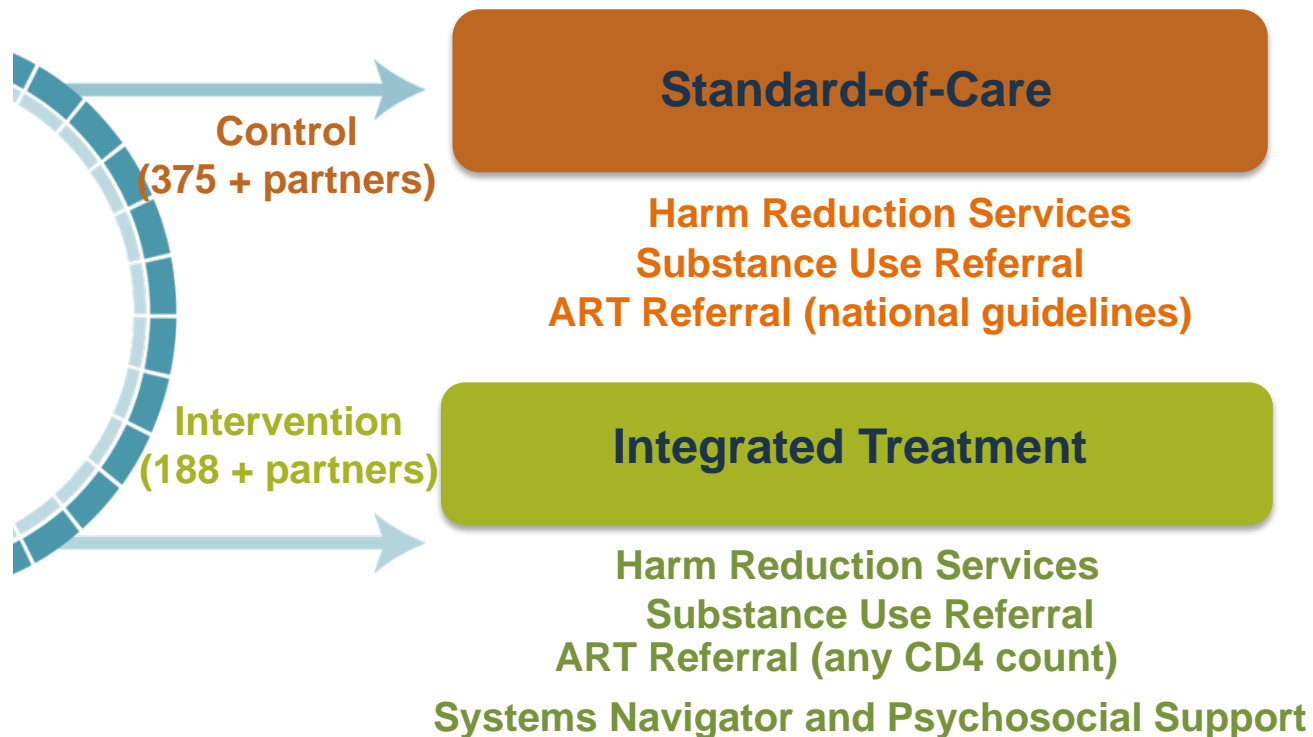
<b>Intervention</b>	<b>Standard of Care</b>
125 HIV +	375 HIV +
188 HIV – Partners	563 HIV – Partners

**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

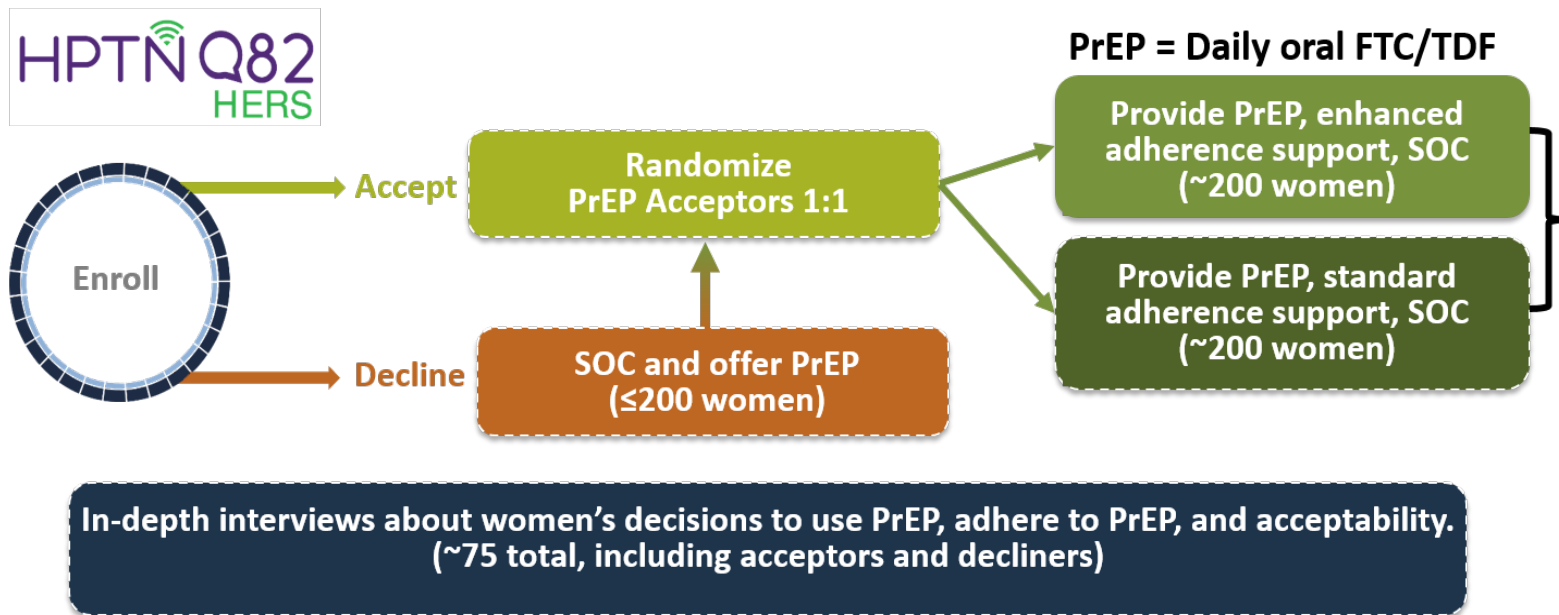


## HPTN 082

### 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



Standard Adherence Support	Enhanced Adherence Support
<ul style="list-style-type: none"> <li>• CBT counseling</li> <li>• SMS texting</li> <li>• Adherence clubs</li> </ul>	<ul style="list-style-type: none"> <li>• CBT counseling</li> <li>• SMS texting</li> <li>• Adherence clubs</li> <li>• <b>Drug level feedback counseling</b></li> </ul>

# HPTN 082: Design & PrEP uptake

## 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

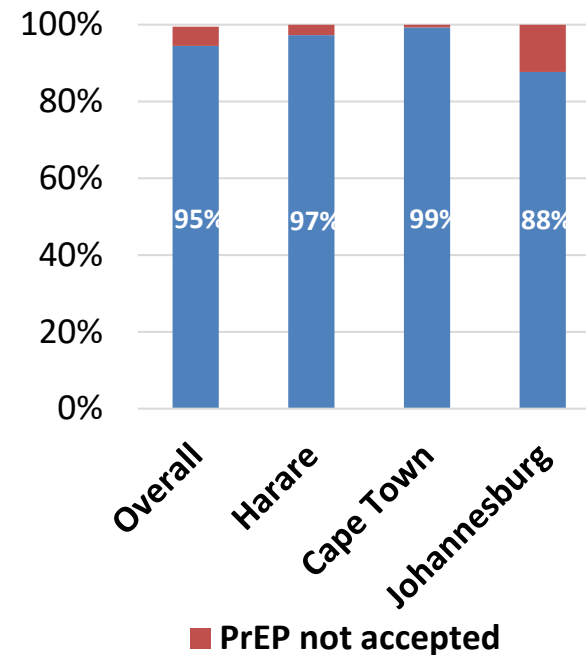
### Target Enrollment

- 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



## 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

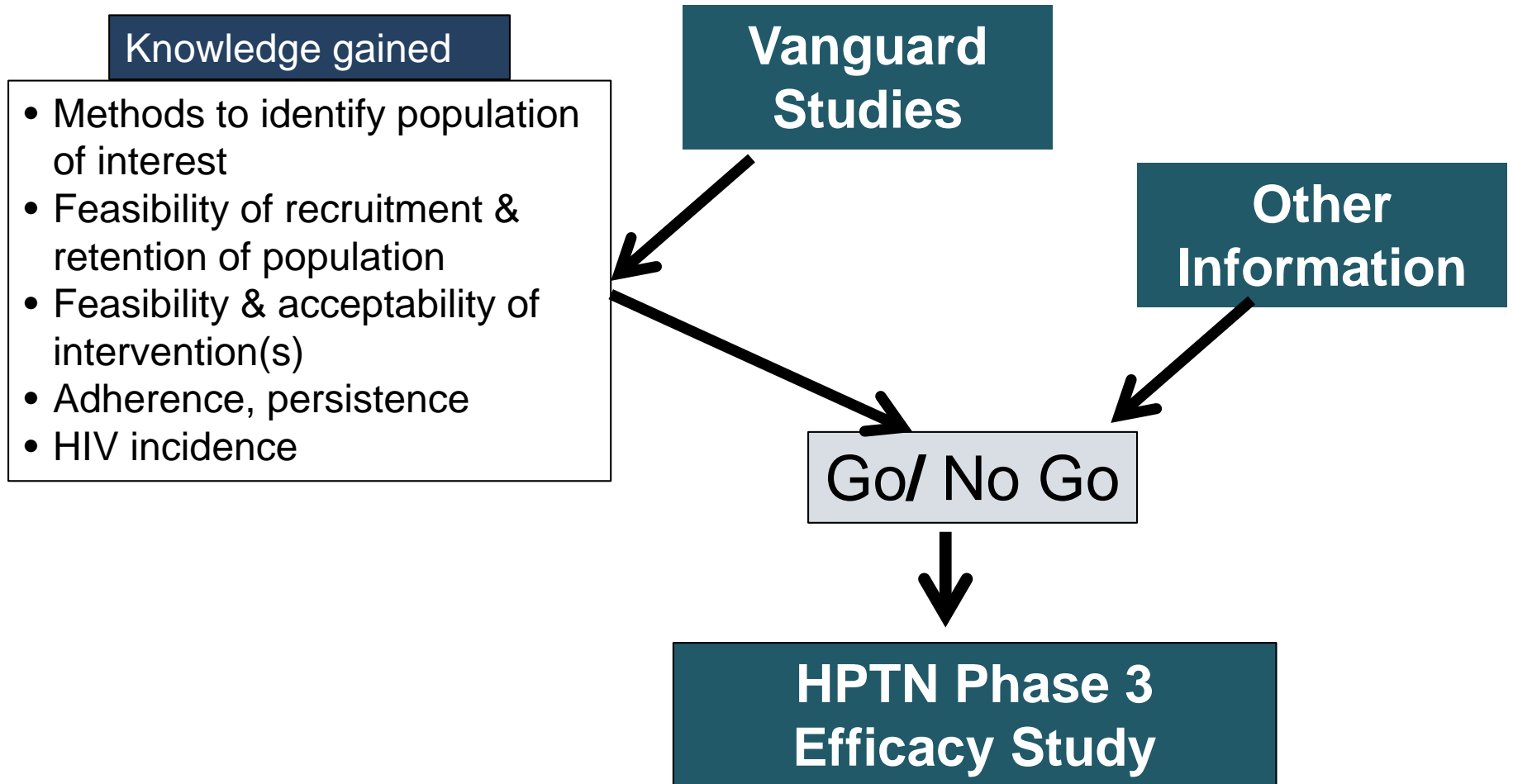
- Methods to identify population of interest
- Feasibility of recruitment & retention of population
- Feasibility & acceptability of intervention(s)
- Adherence, persistence
- HIV incidence

**Vanguard  
Studies**

**Other  
Information**

**Go/ No Go**

**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.

<b>1. Application Date:</b>	
<b>2. Title of the proposed study:</b>	
<b>3. Name and contact information for proposing HPTN Investigator(s) (include institutional affiliation, email, phone):</b>	
<b>4. Number and title of primary HPTN study to which the proposed study is linked:</b>	
<b>5. Name and contact information for non-HPTN Investigator(s) (include institutional affiliation</b>	<input type="checkbox"/> Not applicable <i>Note: All non-HPTN Investigators using biological specimens from HPTN</i>



# 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.

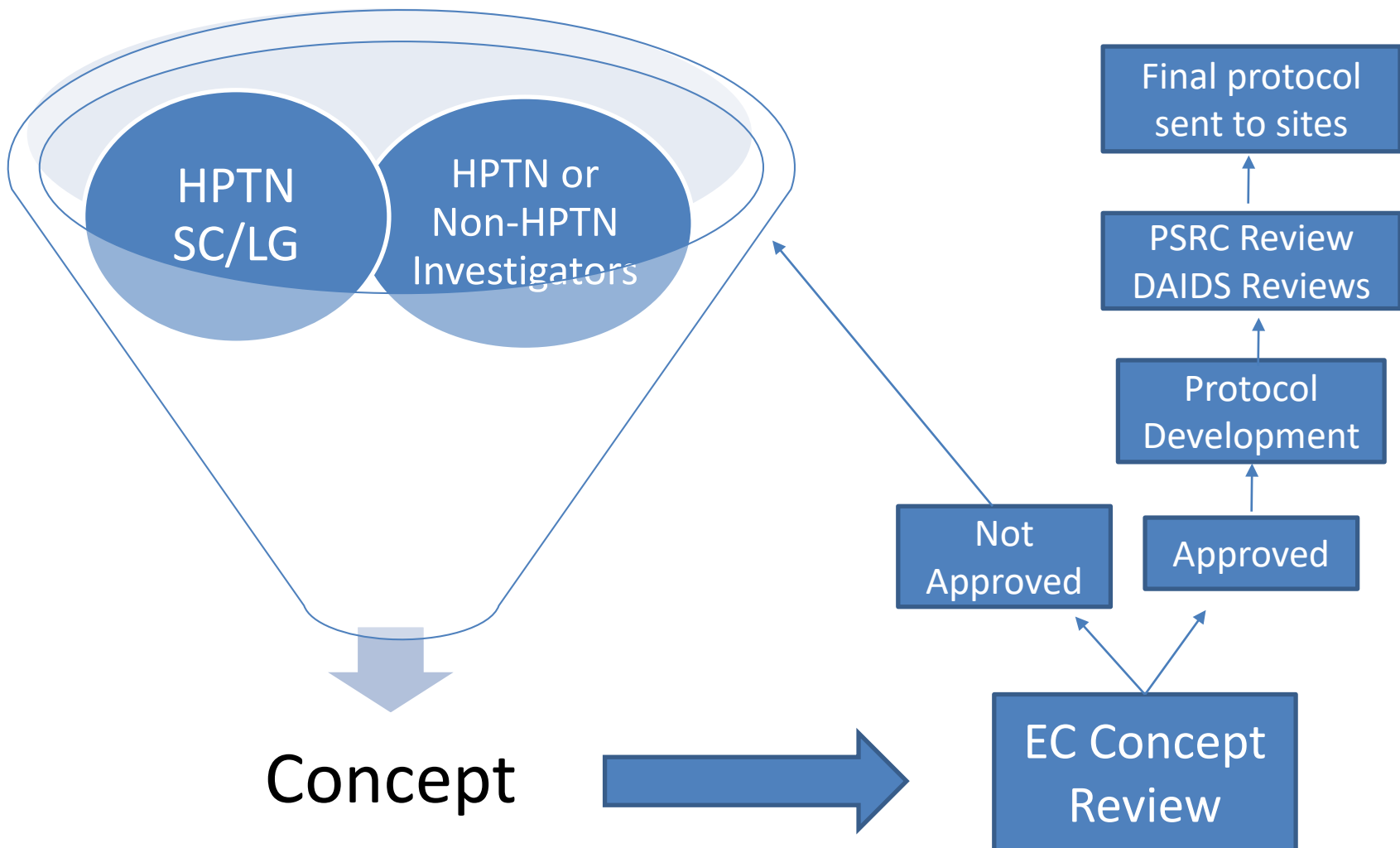
**ACCEPTABILITY AND USE OF PREP PRODUCTS AMONG WOMEN TOOL**

Women at Risk Scientific Committee

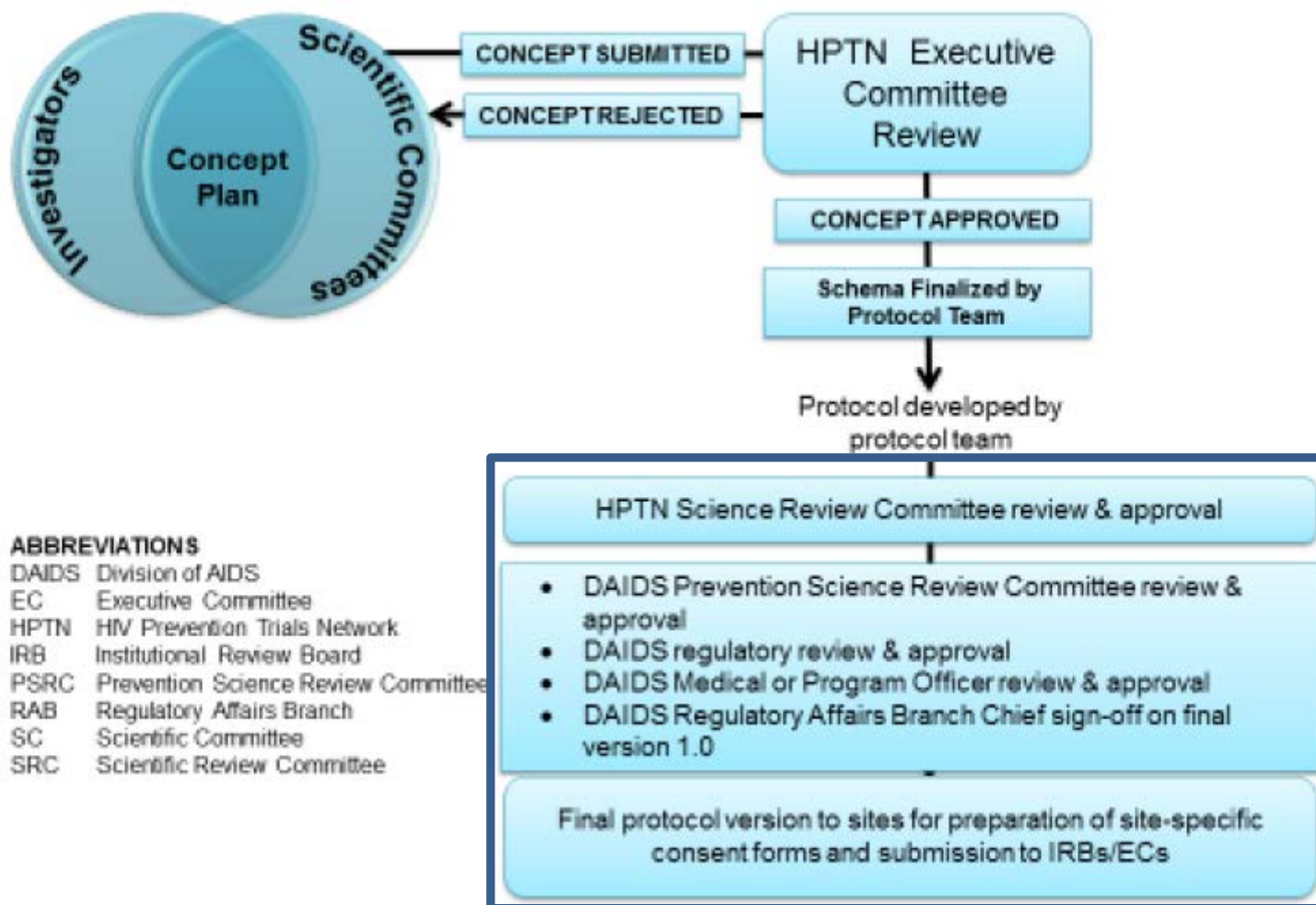
**Building Scientific Expertise in Substance Use-Related Risks for HIV Transmission in  
HPTN Protocols**

**Substance Use Scientific Committee**

# HPTN Science Generation Process



# Science Generation Process



# 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**