

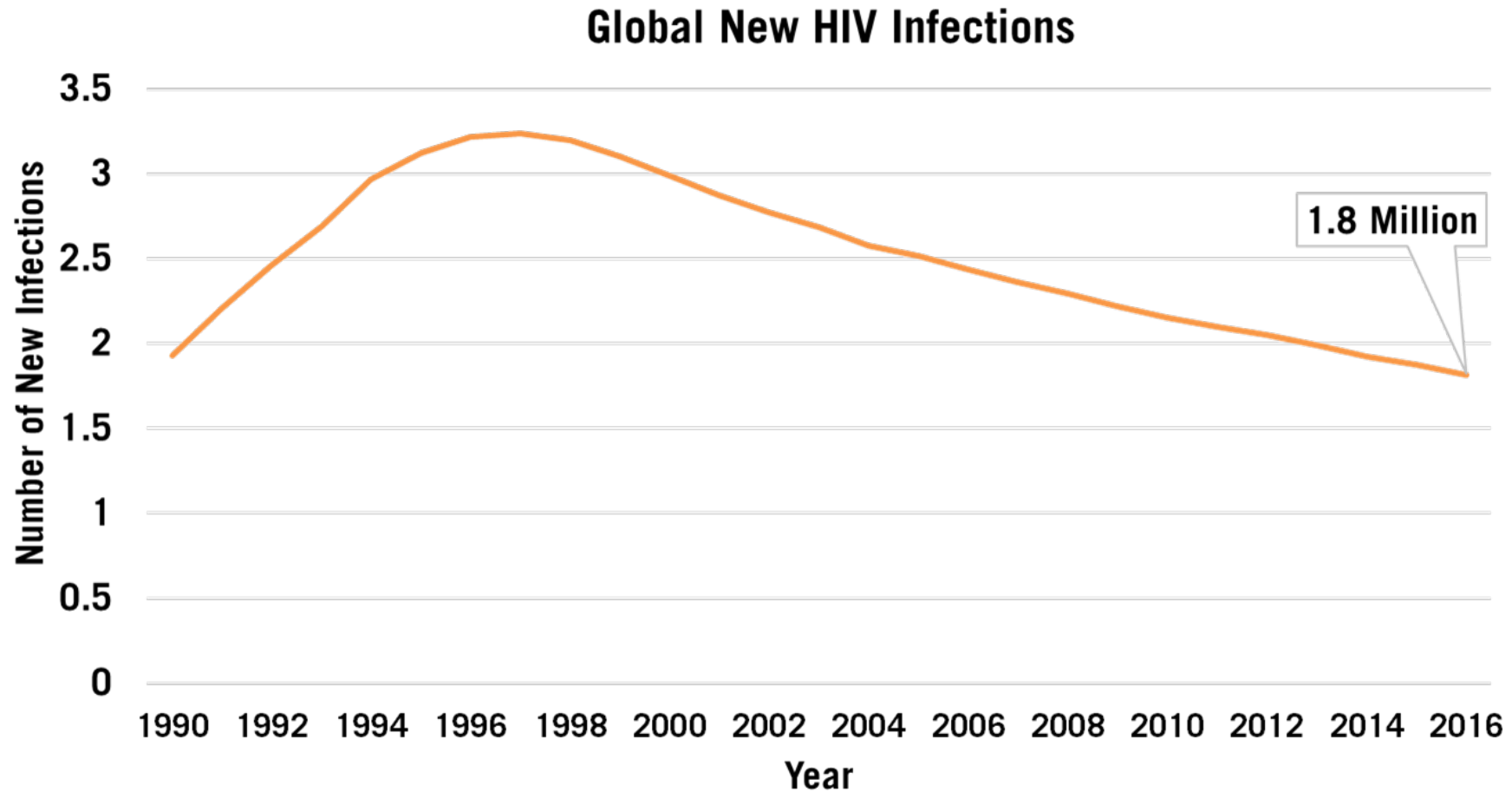
Reviewing the HIV Prevention Landscape and Addressing the HPTN Research Gaps

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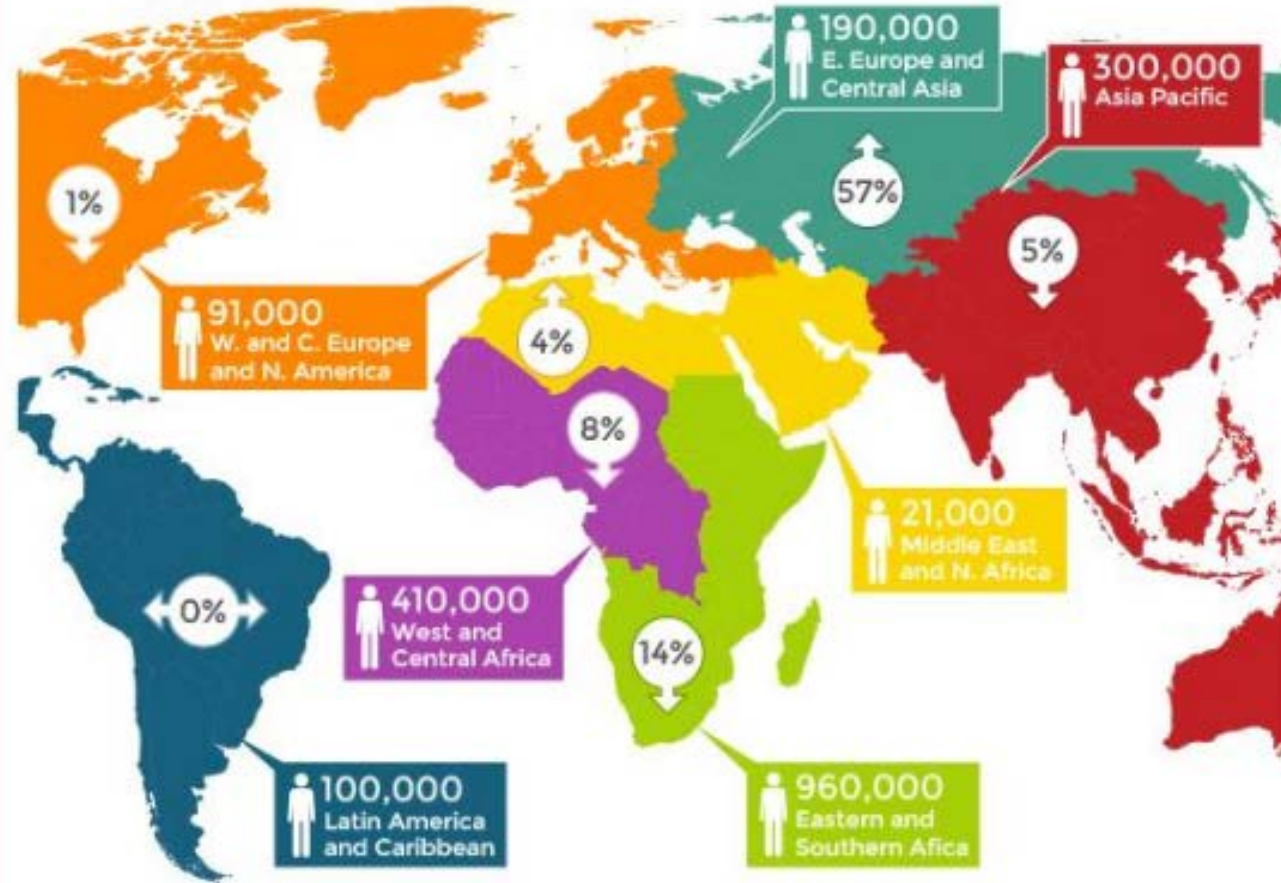
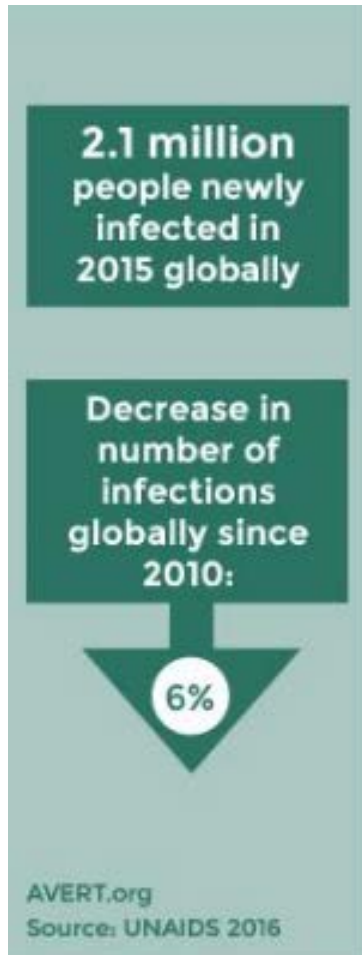
Outline

- Overview of Prevention Landscape
- Overview of HPTN Scientific Agenda
- Operationalizing Research Priorities into Research Studies
- HPTN Concept Sheet

Decline in New Infections



Geographic Hotspots



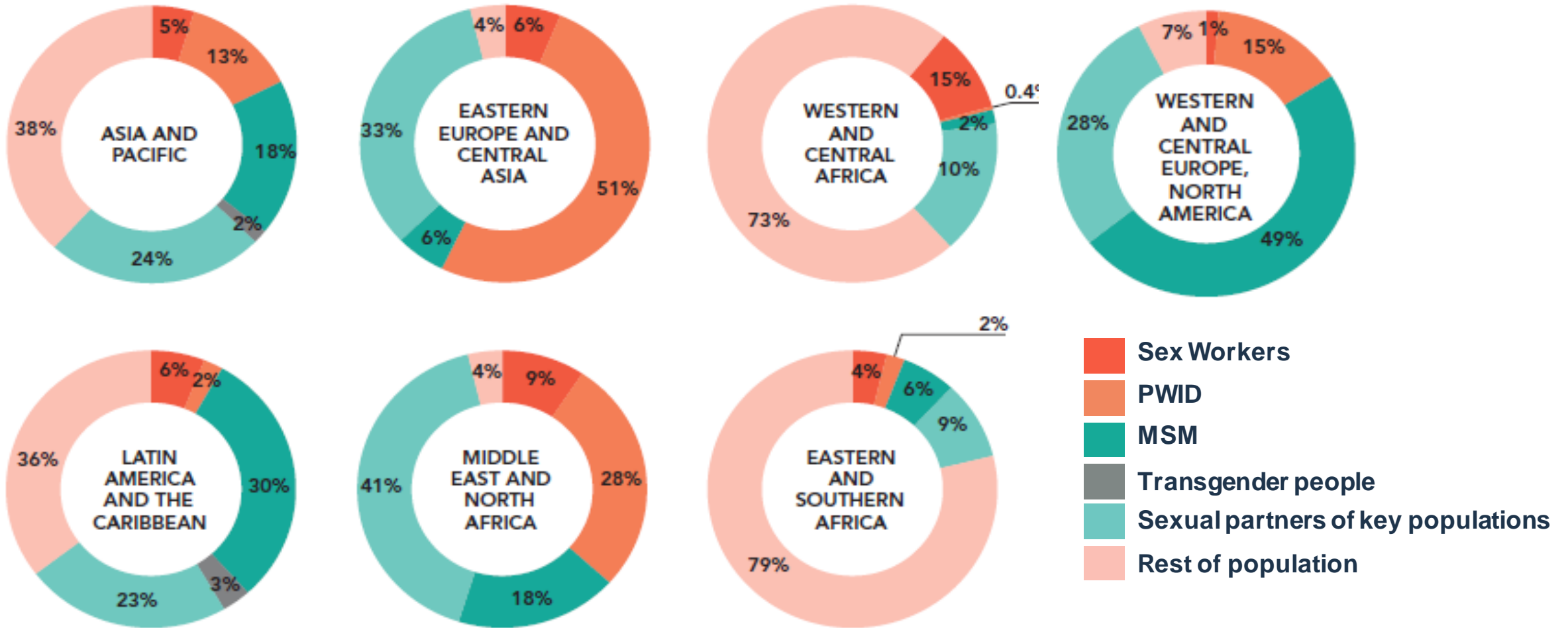
> 40,000 new infections per week

36.7 million

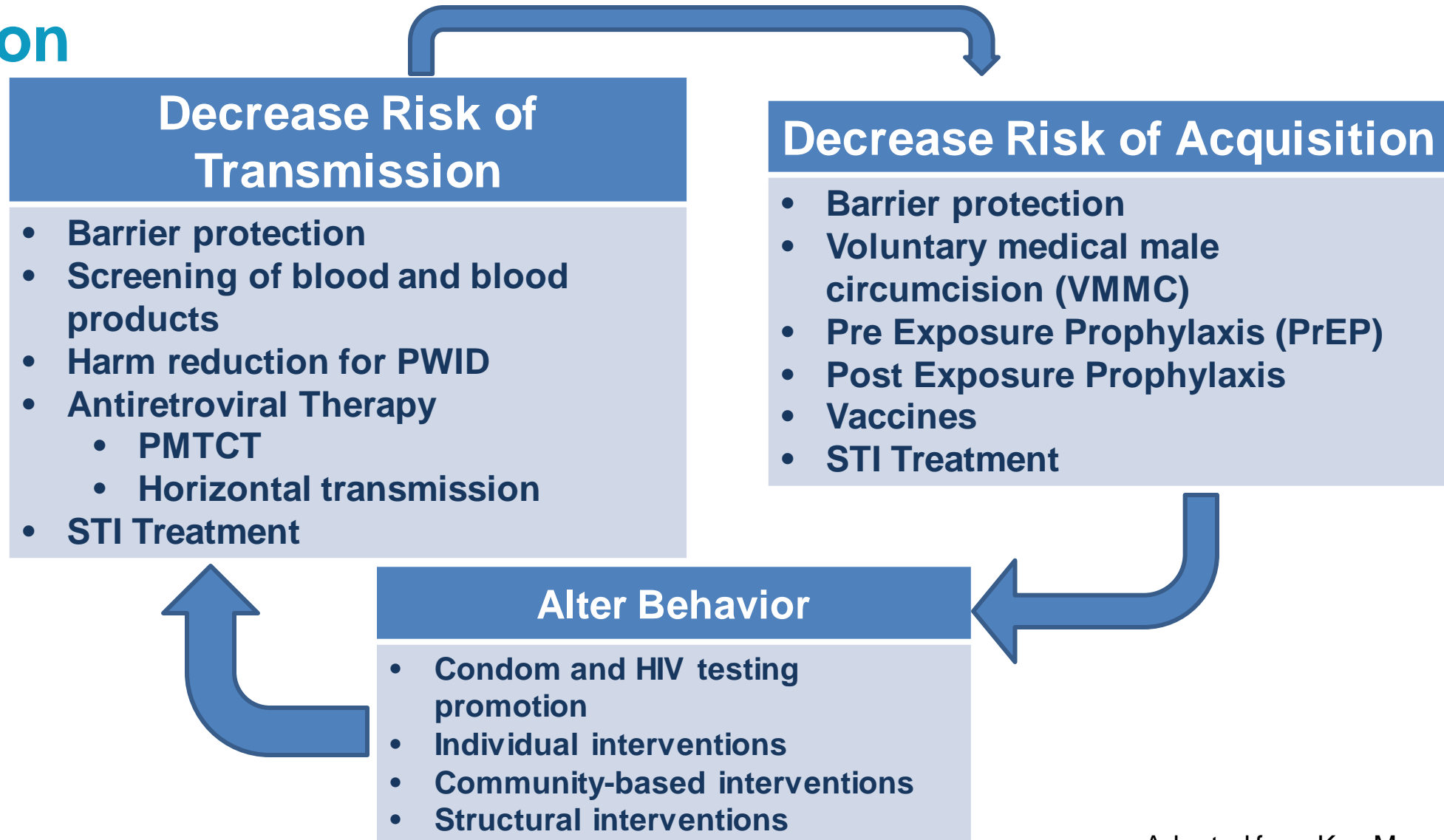
people living with HIV

(UNAIDS 2016)

Priority and key populations



HIV Prevention Approaches and Tools



Biomedical Products for Prevention



Demonstrated Efficacy

VMNC
TasP
Oral PrEP

Submitted for Approval

Vaginal Ring

Under Investigation

Vaccines
Injectable PrEP
AMP
Implant

Can voluntary medical male circumcision be used to prevent HIV acquisition?



- **Design:** RCTs evaluate if circumcision can prevent HIV acquisition in men
- **Studies:**
 - ANRS 1265 (S. Africa): 18-24y men (n= 3,274)
 - Rakai, Uganda: 15-49 y (n=4,996)
 - Kisumu, Kenya: 18-24 y (n=2,784)
- **Results:** Men who were circumcised had a **51-60%** lower incidence of HIV infection than men in the uncircumcised groups

HPTN 052 – Use of ART for Prevention in Serodiscordant Couples

Stable, healthy, serodiscordant couples, sexually active
CD4 count: 350 to 550 cells/mm³



Primary Transmission Endpoint
Virologically-linked partner infections

Primary Clinical Endpoint
WHO stage 4 clinical events, pulmonary tuberculosis, severe bacterial infection and/or death

HPTN 052: Treatment as Prevention



1,763 sero-discordant couples (97% heterosexual)

- HIV infected partners: 890 men, 873 women

+ 39 HIV Transmissions

28 linked HIV
transmissions

Immediate ART:
1 transmission

Delayed ART:
27 transmissions

96% Protection

Can ARVs be used prophylactically to prevent HIV acquisition?



- Design: RCTs conducted in HIV negative populations evaluating oral pre exposure prophylaxis

	% of blood samples with tenofovir detected	HIV protection efficacy in randomized comparison
iPrEx	51%	44%
Partners PrEP FTC/TDF arm	81%	75%

Effectiveness is correlated with adherence

Can a vaginal ring be used to delivery topical PrEP to women?

- Vaginal ring (VR) containing dapivirine (DPV) is under evaluation for pre-exposure prophylaxis (PrEP) for HIV prevention among women



ASPIRE



Behavioral Interventions for Prevention of HIV Acquisition



- Decrease risk behaviors
- Increase protective behaviors
- Increase uptake and adherence to biomedical products


Harm Reduction

- Needle and Syringe Exchange Programs
- Medically Assisted Therapy

Counseling

Socioeconomic interventions

HPTN 068: Effects of Cash Transfer For the Prevention of HIV in Young South African Women

Enrollment	2,537  13-20 yrs
Intervention	Control
1,263	1,274
Cash transfer conditional on school attendance	No cash



Primary outcome: Primary HIV Incidence

HPTN 068: Key Findings

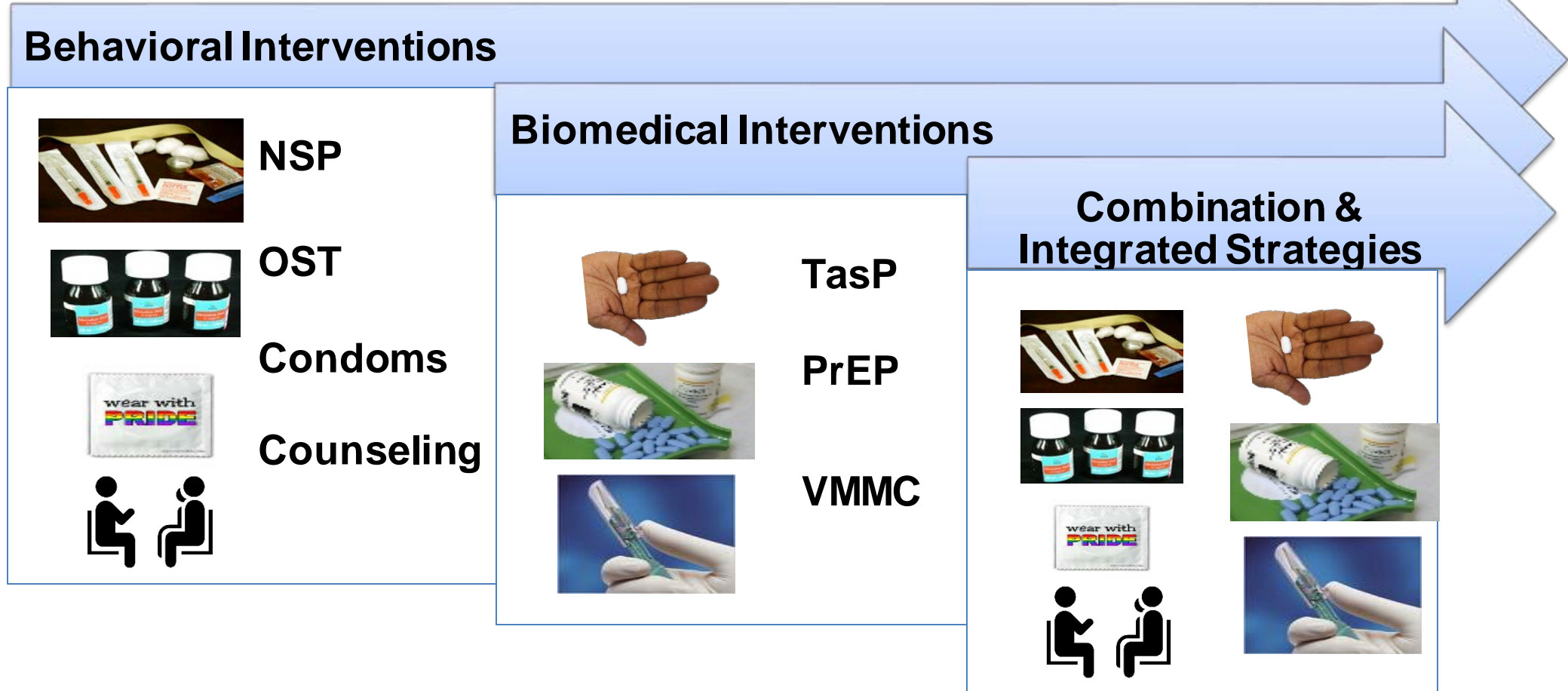
Incidence Outcomes

- **Overall HIV Incidence: 1.8%**
 - Among 16 year olds: 1%
 - >20 years: 5%
- **No difference in HIV incidence**
- **No difference in HSV-2 incidence**

School Attendance Outcomes

- **High school attendance in both study arms was high**
 - Three fold high risk of HIV infection in school drop out to non-drop outs
- **School enrollment and attendance were protective for HIV acquisition irrespective of study arm**

Optimizing Intervention Efficacy



Overview of HPTN Scientific Agenda

- Integrated Strategies Agenda
 - TasP (HPTN 071, HPTN 074, HPTN 078)
- PrEP Agenda
 - Optimizing oral PrEP (HPTN 073, HPTN 082)
 - New PrEP (HPTN 083, HPTN 084, HPTN 086, AMP, other phase I bNAbs)
- Recruitment Feasibility
 - HPTN 075

HPTN 071 - PopART

- Community-based, RCT evaluating the impact of a combination HIV prevention package on HIV incidence
- Total estimated 1 million participants testing TREATMENT as PREVENTION on a community Level

Arm A/B	Arm C
Full PopART intervention ART irrespective of CD4 count or clinical stage	Standard of care at current service provision levels, including ART irrespective of CD4 count or clinical stage

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

HPTN 071 PopART Interventions

- Intervention Arm Components delivered by Community HIV Care Providers (CHiPs):
 - Offering voluntary HIV counseling and testing annually through a house-to-house campaign
 - Linking those with HIV to care at the local health center
 - Offering ART to all those who are HIV-infected, irrespective of CD4+ count or clinical stage
 - Promoting voluntary medical male circumcision (VMMC) for men who test HIV-negative
 - Promoting services for the prevention of mother-to-child transmission (PMTCT) to HIV-infected pregnant women
 - Referral for treatment of sexually transmitted infections
 - Providing condoms in the community
 - Screening and referral for tuberculosis (TB)

HPTN 074: Can TasP be used to prevent HIV acquisition in PWID?

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

Results:

- 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:.



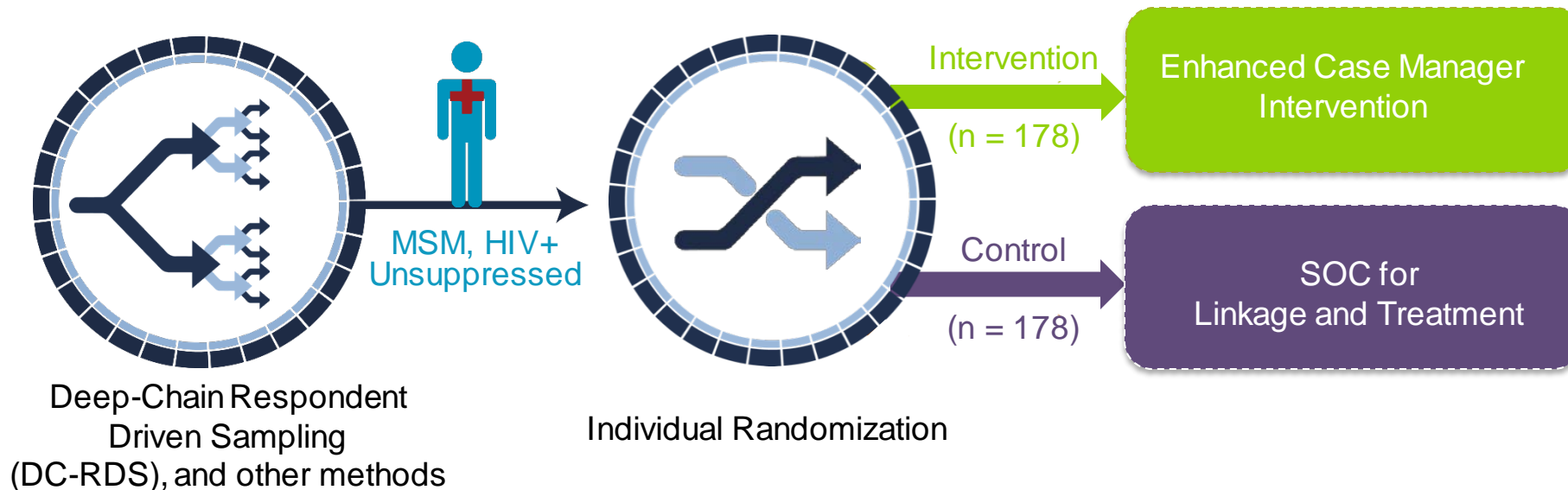
Intervention	Standard of Care
125 HIV +	375 HIV +
188 HIV – Partners	563 HIV – Partners

**15 Months Recruitment
12 Months Follow-Up**

HPTN 078: Can an integrated strategy using TasP be used to help HIV infected MSM achieve and maintain viral suppression?

Enhancing Recruitment, Linkage to Care and Treatment for HIV-Infected Men Who Have Sex with Men (MSM) in the United States

Study Design



HPTN 073: Can we optimize oral PrEP for black MSM?

- **Study was designed to answer:**
 - 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?
- **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
 - Engagement of HPTN Black Caucus advantageous in design and implementation of the study

HPTN 082: Can we optimize oral PrEP for young women?

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

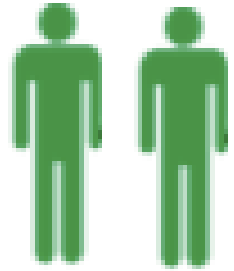
Target Enrollment

- 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

HPTN 075: Can African MSM be recruited into a prevention research study?



Feasibility & Acceptability

Preliminary Results:

- Recruiting and retention of MSM from sub-Saharan Africa is feasible
- With sufficient preparation such studies can be implemented minimizing social harms
- Implementing studies with this population enables acceptance by healthcare workers and CABs.

Long-acting Agents for HIV Prevention

Long-acting injectable ARVs



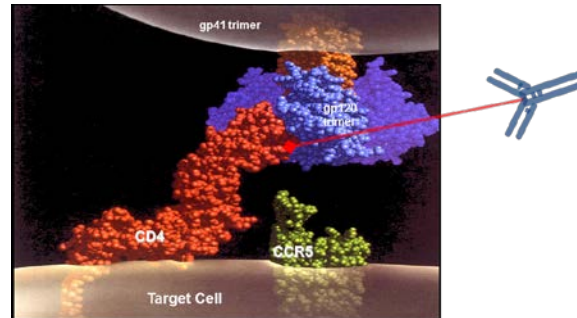
Cabotegravir:

HPTN 083

HPTN 084

HPTN 086

Broadly-neutralizing antibodies



VRC01:

HVTN 703/HPTN 081

HVTN 704/HPTN 085

Other BNABs

HVTN 127/HPTN 087

HVTN 129/HPTN 088

HVTN 130/HPTN 089

Implants



SLAP

HPTN ???

Additional Priority Populations

- Continue work with MSM, substance users, and women of child bearing age (**HPTN 075, HPTN 078, AMP, HPTN 074, HPTN 083, HPTN 084**)
- Set protocol specific or country specific enrollment quotas for populations deemed most vulnerable (**HPTN 083**)
- Heterosexual men in Africa (**HPTN 071**)
- Research focusing on and inclusive of transgender people (including transgender men) (**HPTN 083, AMP**)

HIV Prevention Package

- Include discussions of viral suppression for all participants (regardless of sero-status) enrolled in research conducted by the HPTN
 - **HPTN 052, TasP (071, 074, 078)**
- Establish PrEP access as part of the HIV prevention package for research conducted by the HPTN

Behavioral Research

- Include strong behavioral components with biomedical research
 - In all studies, what are new/additional behavioral interventions not being included
- Utilize results from research to develop demonstration projects (i.e. HPTN 073)
- Focused research on chemical sex and blood sharing (blue-toothing)

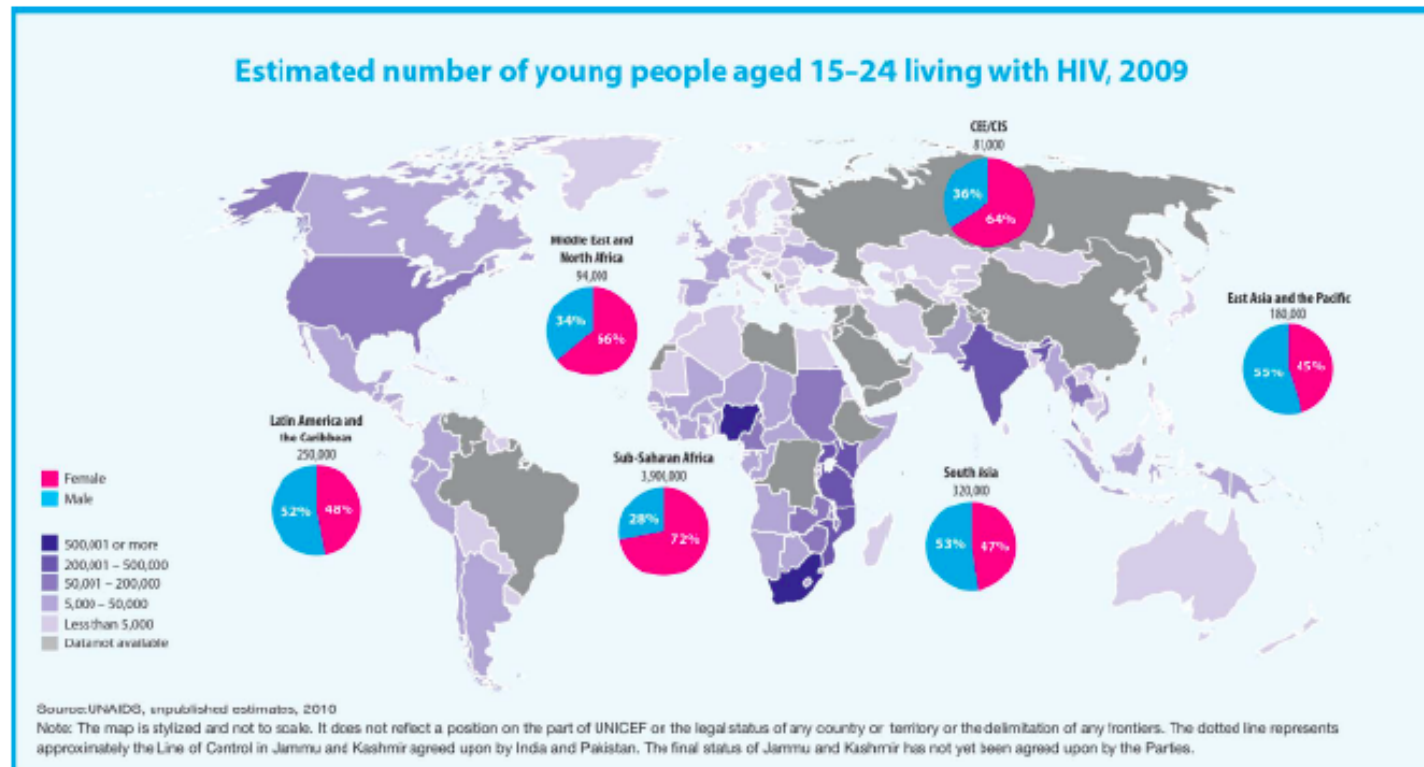
Questions?

Operationalizing Epidemic Priorities into Research Studies

- Example:
 - Young Women and Adolescents in sub-Saharan Africa

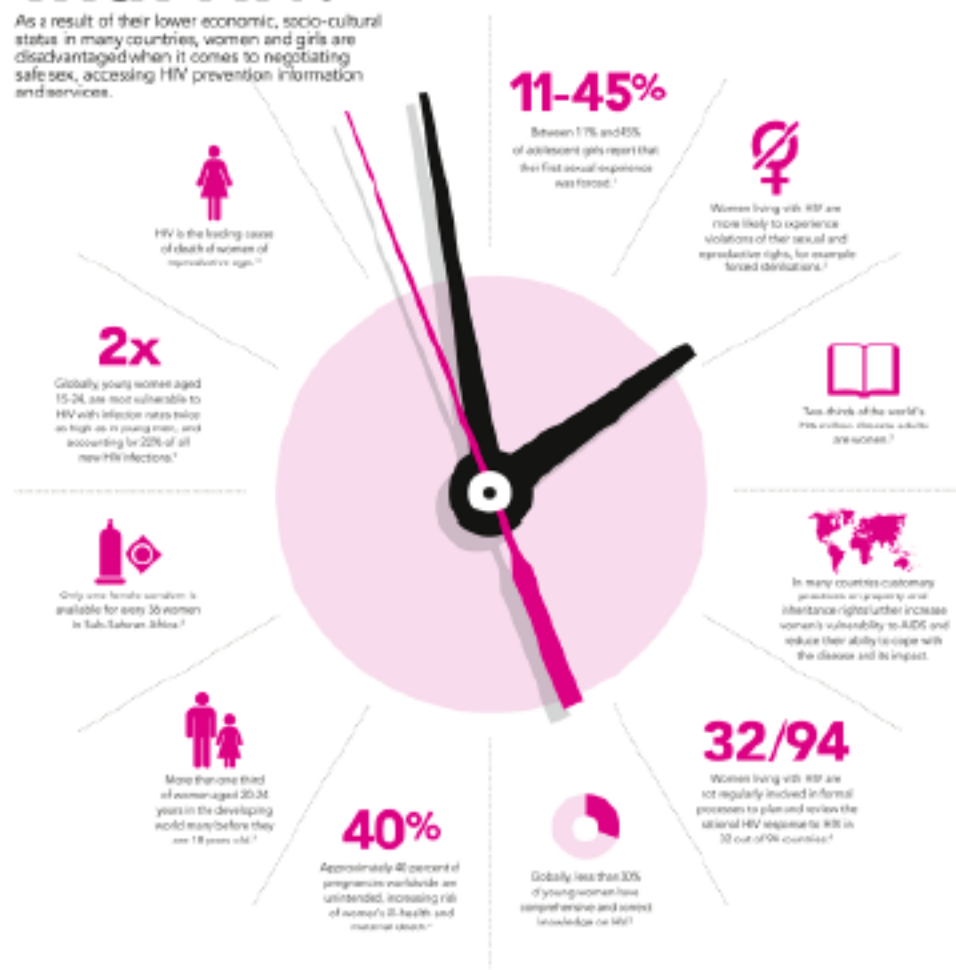
3.9 million young people in SSA aged 15-24 years are living with HIV

Three-quarters are young women



Every minute, a young woman is newly infected with HIV.

As a result of their lower economic, socio-cultural status in many countries, women and girls are disadvantaged when it comes to negotiating safe sex, accessing HIV prevention information and services.



Sources

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2. Gender inequality, UNAIDS, 2010
3. Rapid Assessment of HIV, 2010
4. Gender inequality, UNAIDS, 2010
5. UNAIDS Report on the Global AIDS Epidemic, 2010

6. East et al., Alliance for the Girls and Young Women: Improving Planning and Policy and Reducing Risk, New York, Guttmacher Institute, 2008
7. UNAIDS, The State of the World's Children 2010, Adolescence: A period of opportunity, New York, 2010
8. 2010 Mid-Year Report, Comprehensive Gender Programming - July 2010

9. UNAIDS/WHO AIDS, 2010
10. <http://www.unaids.org/hi/hiindex.asp>, 2010, 2011

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PrEP as part of combination for young women in SSA

- How do you create demand?
 - Motivations and characteristics of young women who accept PrEP
- How do you support effective use?
 - What does adherence support look like for young women?
 - Counselling, SMS, clubs
 - Drug feedback levels
 - Targeted/intensification for those who need more support?

Translating epidemic priority to research studies

HPTN 082: Design

HPTN 082: Evaluation of daily oral PrEP as a primary prevention strategy for young African women

Study Population

Uninfected women
Ages 16-25 yrs

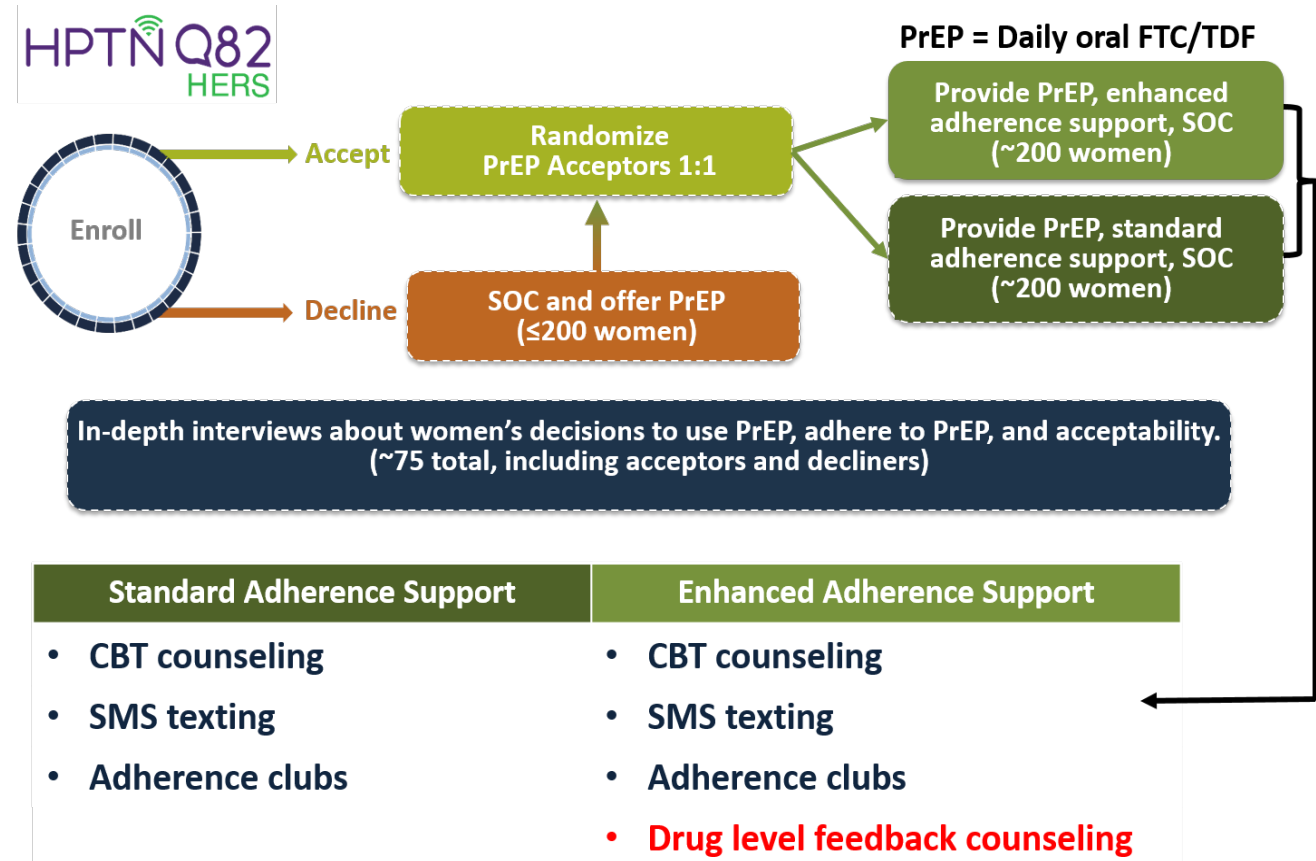
Johannesburg & Cape Town,
South Africa
Harare, Zimbabwe

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



Overview of HIV Prevention Landscape

- Where should we focus our resources?
 - Geographic Hotspots
 - Priority and key populations
- What are our available tools?
 - Biomedical Interventions
 - Behavioral Interventions
 - Combination/Integrated Strategies

Summary of Purpose and Rationale

- This should include introduction and background literature to set the context of the proposed research
- Specify the principal aim(s), rationale, relevant background, overall design for Phase I/II trials
- Describe critical pathway to efficacy evaluation
- Indicate relevance to the long-term global goals of HPTN

Study Design

- Specify the type of study proposed, e.g., whether it is a Phase I, IIA, IIB, or III randomized clinical trial, observational, nested case control study, etc.

Description of the Intervention

- Describe intervention (e.g. drug/regimen, counseling program), specify study arms, including control if applicable

Endpoints

- Specify the primary endpoints such as seroconversion, dose-limiting toxicity, specific behavioral outcomes (either primary or secondary endpoints).

Study Population

- Specify sample size, the principal inclusion and exclusion criteria, recruitment source (s), appropriateness of the proposed study population for the proposed concept, and other salient characteristics

Product-related Considerations

- Is an IND needed?
- Is the product and placebo available in sufficient quantity for the proposed study?
- From whom?
- Is there a plan to manufacture sufficient quantities for any proposed follow-on studies?

Timeframe

- Specify expected duration of accrual and follow-up, and any contingencies for development/implementation (e.g. final product selection/dosage to await results of ongoing study)

HPTN 082

- Brief background - high annual HIV incidence rates of 5-6%
- Rationale – if PrEP delivered with supportive interventions, adherence will improve and PrEP will be efficacious
- Target population - HIV-uninfected women at risk 16-25 years
- Study design – offer open label PrEP, counseling, SMS, adherence clubs, drug level feedback (per randomization)
- Key outcomes – PrEP uptake and adherence
- Study assessments – behavioral data, uptake, ARV drug levels
- Estimated sample size – 400 who accept PrEP at enrollment, up to 200 decline PrEP at enrollment
- Potential impact on the target population – will identify key elements to maximize uptake and adherence to oral PrEP

Science Generation of Concepts to Protocols

Scientific Committees

Concept Plan

Concept Not Approved

HPTN EC
Reviews and Scores

Concept Approved

Protocol Development
by Protocol Team

HPTN SRC
Review and Approval

- DAIDS PSRC review and approval
- DAIDS regulatory review and approval
- DAIDS medical or program officer review and approval
- DAIDS RAB 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

ACKNOWLEDGEMENTS

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