



HPTN
HIV Prevention
Trials Network

HPTN 082 and PrEP Research in Africa

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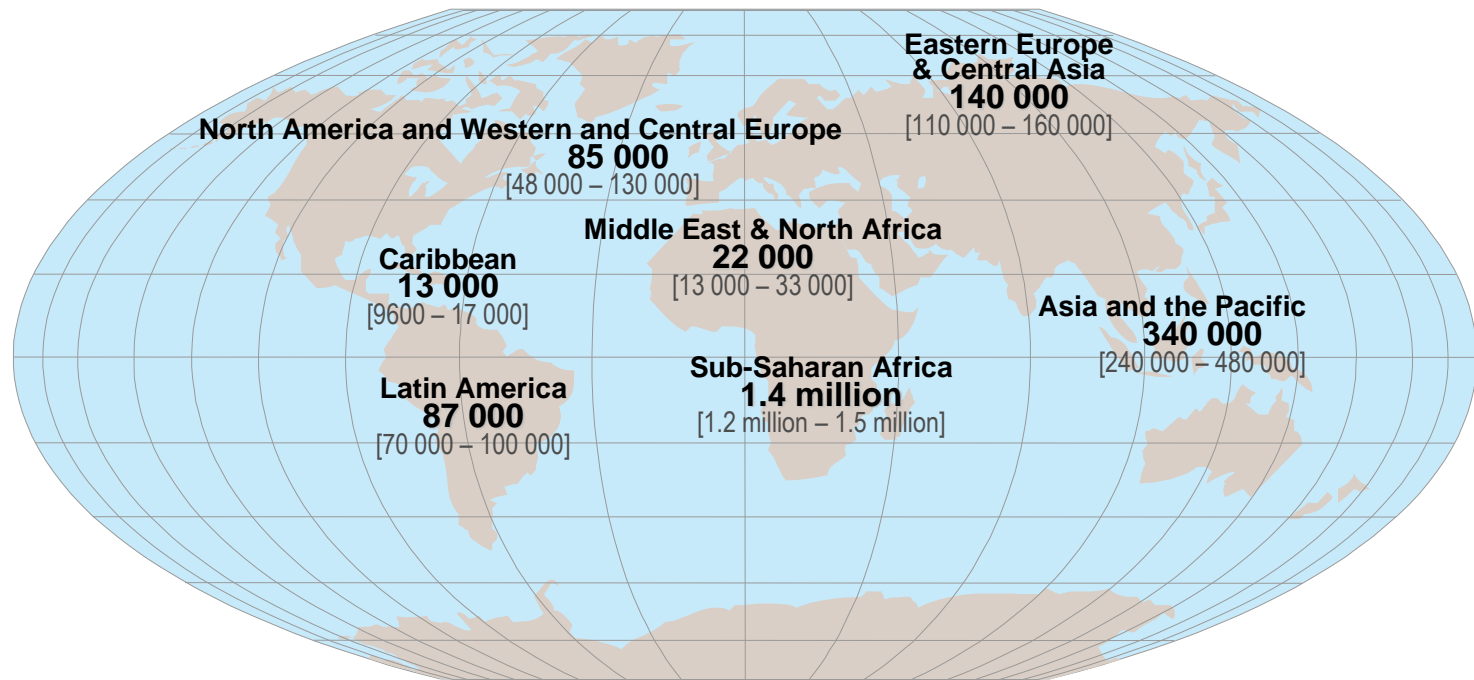
On behalf of the HPTN 082 team

June 12, 2016

Outline

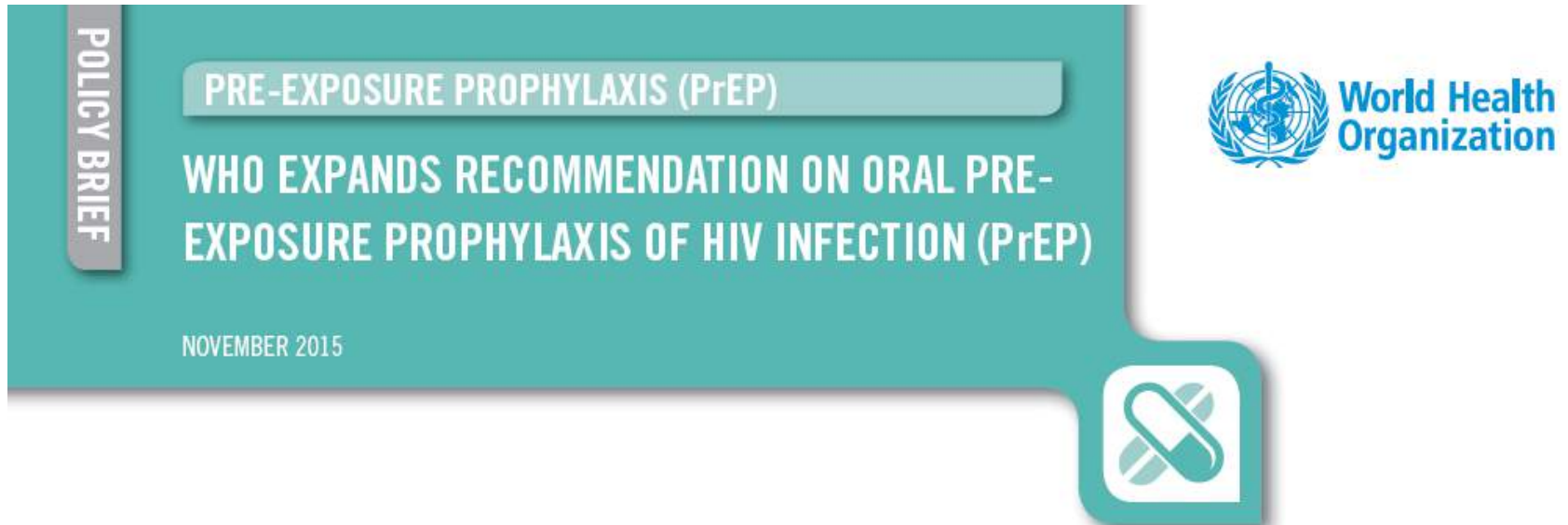
- PrEP in Africa
 - Evidence
 - Potential impact
 - Progress to date on the continent
- Oral PrEP for adolescent girls and young women

We need to prevent new HIV infections



Total: 2.0 million [1.9 million – 2.2 million]

Estimated number of people newly infected with HIV | 2014



In November 2015, WHO recommended that oral PrEP be offered to individuals at substantial risk of HIV infection as part of combination HIV prevention approaches

What is PrEP?

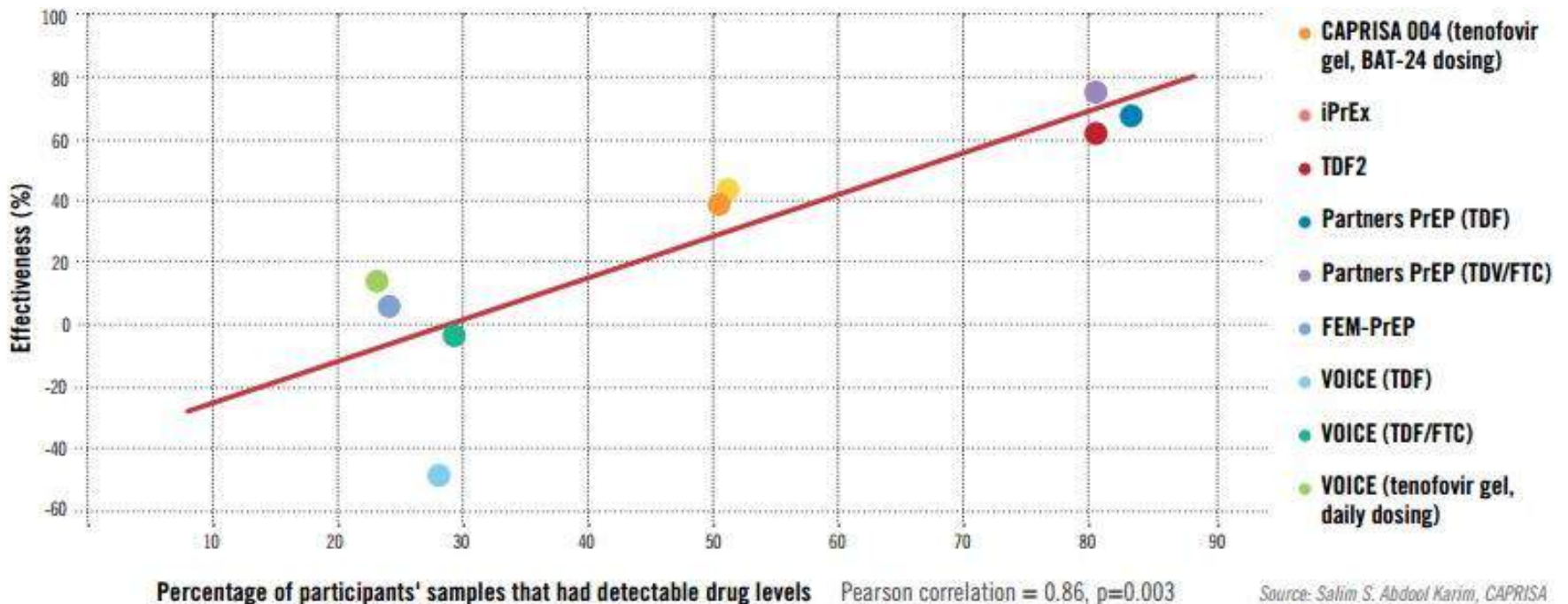
- Pre-Exposure Prophylaxis:
 - is the use of antiretroviral (ARV) drugs by people who do not have HIV infection in order to prevent infection with HIV
 - E.g. malaria prevention, contraceptive pills
- Tenofovir disoproxyl fumarate (TDF)
 - Safe and well-tolerated
 - Daily dosing of co-formulated tablet supported by PK/PD
 - Relatively high barrier to resistance
 - Rapid concentration in genital/rectal tissues
 - Animal models suggest that TDF + FTC offers better protection than TDF alone



PrEP – key evidence

- 12 randomised controlled trials of oral PrEP effectiveness conducted in a range of different populations worldwide
- PrEP was effective in reducing HIV risk across age, gender, ARV regimen (TDF versus emtricitabine (FTC) + TDF) or mode of acquiring HIV (rectal or penile/ vaginal).
- Rates of adverse events did not differ between PrEP and placebo
- Resistance was low (1 in 1000)

PrEP works, when taken



HIV risk was reduced by 70% in trials where adherence as $\geq 80\%$.

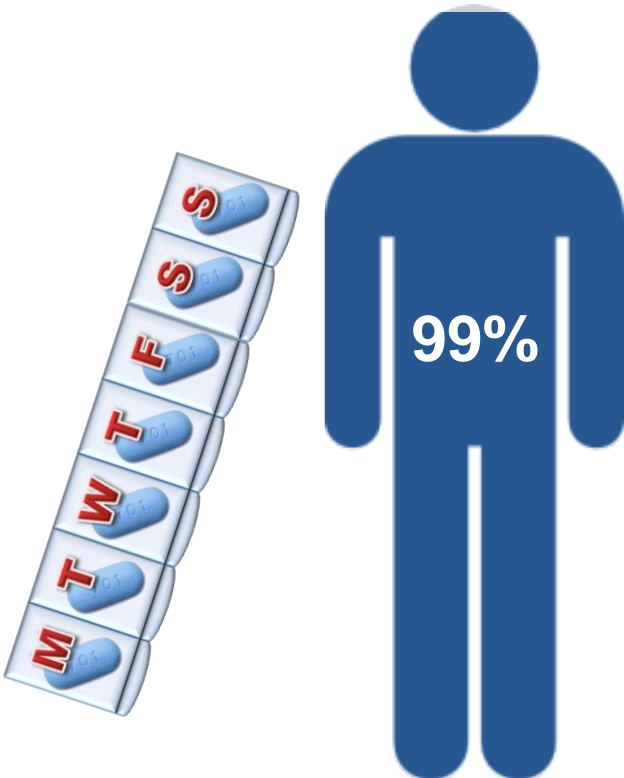
Understanding lack of efficacy of oral PrEP in trials in women

TRIAL	POPULATION	LOCATION	Active arm(s)	EFFICACY (mITT-analysis)
FEM-PrEP	2120 heterosexual women	Kenya, Tanzania, Zimbabwe, South Africa	FTC/TDF	6% (p=0.8) <i>Stopped early due to lack of efficacy</i>
VOICE	3019 heterosexual women	Uganda, Zimbabwe, South Africa	FTC/TDF TDF	-4% (p>0.2) -49% (p=0.07)

- **Low adherence: <30% with tenofovir detected**
 - *Low HIV risk perception?*
 - *Lack of interest in HIV prevention?*
 - *Inability to take a daily pill?*
 - *Lack of motivation in a placebo-controlled trial with an unproven product?*

Maximizing the Potential Effectiveness

TDF/FTC (7x/week)

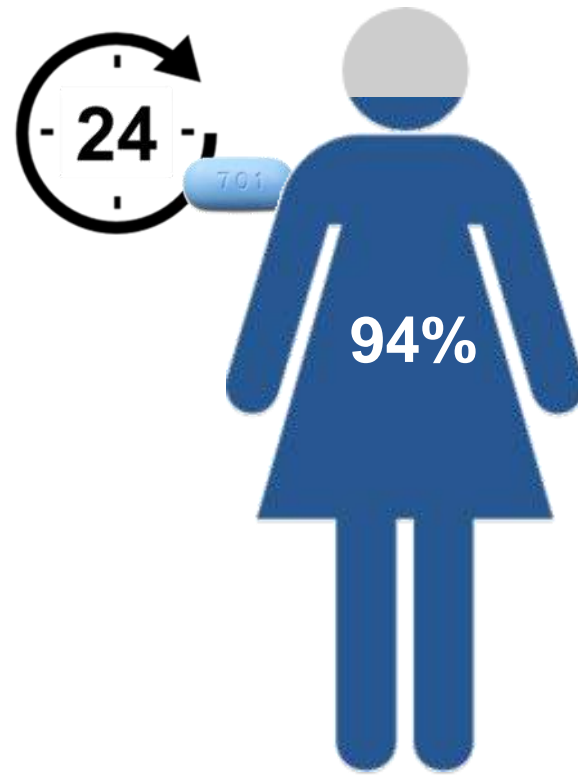


CI: 96 - 99

**Some adherence forgiveness with
retained protection**

Anderson P *et al*, Sci Transl Med. 2012.

TDF/FTC (~1x/24^h)



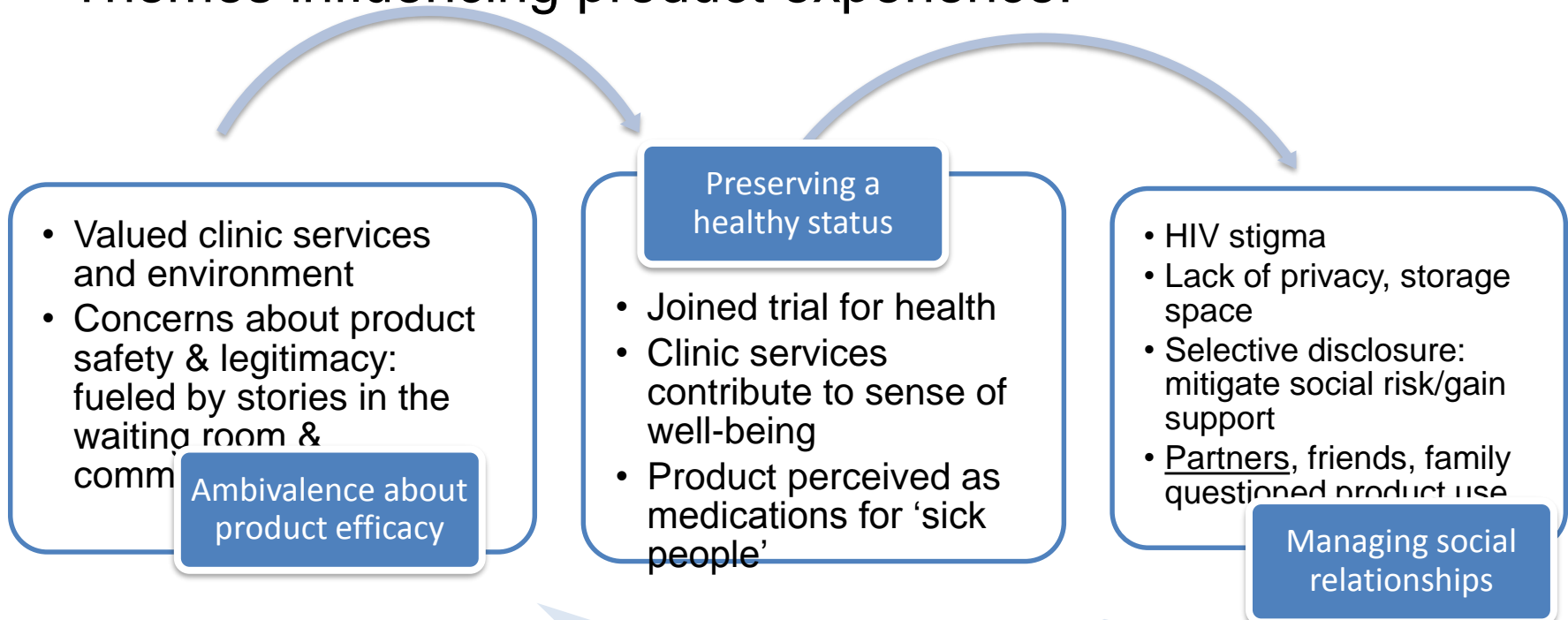
CI: -17 - 100

**6-7 doses per week likely
required**

Donnell D *et al*, JAIDS. 2014.
Cottrell ML *et al*, R4P, 2014.

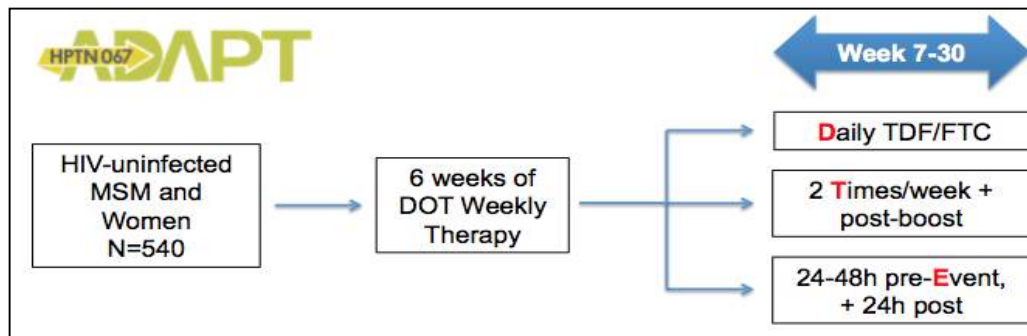
VOICE-C Key Findings

- Demographics similar to VOICE ppts at Johannesburg site
- Difficult to acknowledge product non-use, even in qualitative IDIs
- Themes influencing product experience:



HPTN 067/ADAPT

- 179 women in Cape Town; 6 wks of DOT then randomized to daily, or twice weekly with a post-sex boost or event-driven oral PrEP



- Median age 26 years (range 18-52),
 - 80% were unmarried
 - 83% unemployed
- Adherence (measured by Wisepill & tenofovir levels) & coverage of sex acts highest with daily dosing
 - 75% of sex acts with daily vs 48% with twice weekly/sex boost dose & 52% with event-driven dosing
 - In the daily dosing study arm, 93% of the women had drug in their plasma at week 10, and 79% at week 30

PrEP – who will benefit

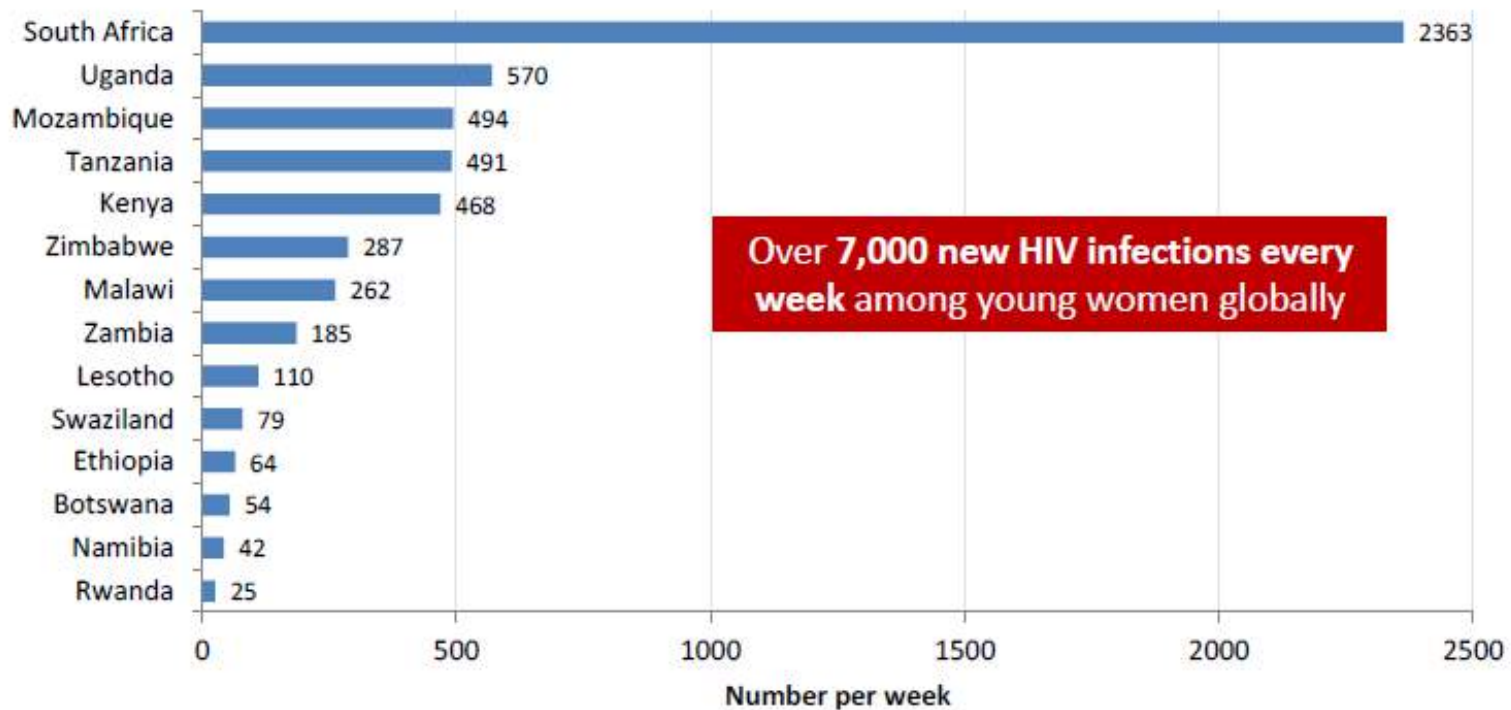


- Greatest impact and cost-effectiveness of PrEP will be greatest in populations with HIV incidence ≥ 3 per 100 person-years.
 - Incidence is ≥ 3 per 100 person-years in at least one age/sex group in Kenya, Lesotho, Mozambique, South Africa, Swaziland and Uganda
- Serodiscordant couples, key populations and adolescent girls and young women

One-third of new infections globally occur in young African women

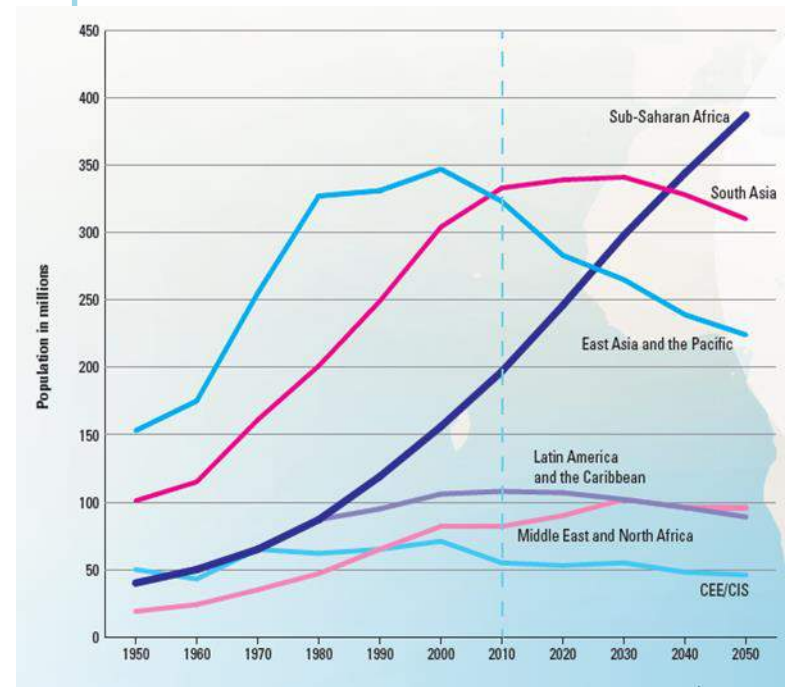
Estimated number of new HIV infections *per week* among young women aged 15-24 years in East and Southern Africa, 2012

Data source: UNAIDS 2013



Fast track HIV prevention for young women

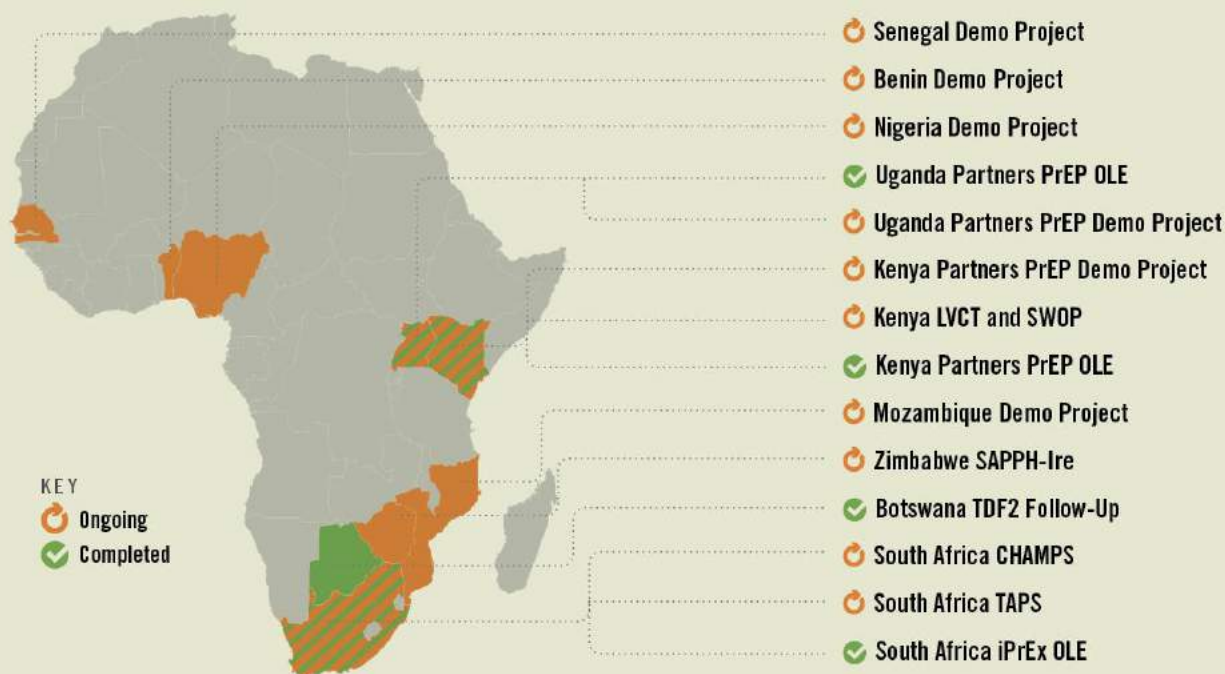
- By 2050, Sub-Saharan Africa is project to have more adolescents than any other region
- This represents an absolute increased in the HIV susceptible population
- More will need to be done to achieve the Fast Track targets by 2030



Population of adolescents 10-19 years old in millions, by region, 1950-2010

Source: UNICEF, 2012

What to Expect for PrEP in Africa in 2015



The above projects involve a range of populations, including sex workers, young people, gay men and other MSM and women and men in serodiscordant couples. Not all countries are gathering data in all populations, but the picture of what PrEP can mean in an African context will get clearer as data begin to come in.

AVAC Report 2014/15: Prevention on the Line
www.avac.org/report2014-15/graphics

By 2016, there are >20 demonstration projects involving PrEP in Africa

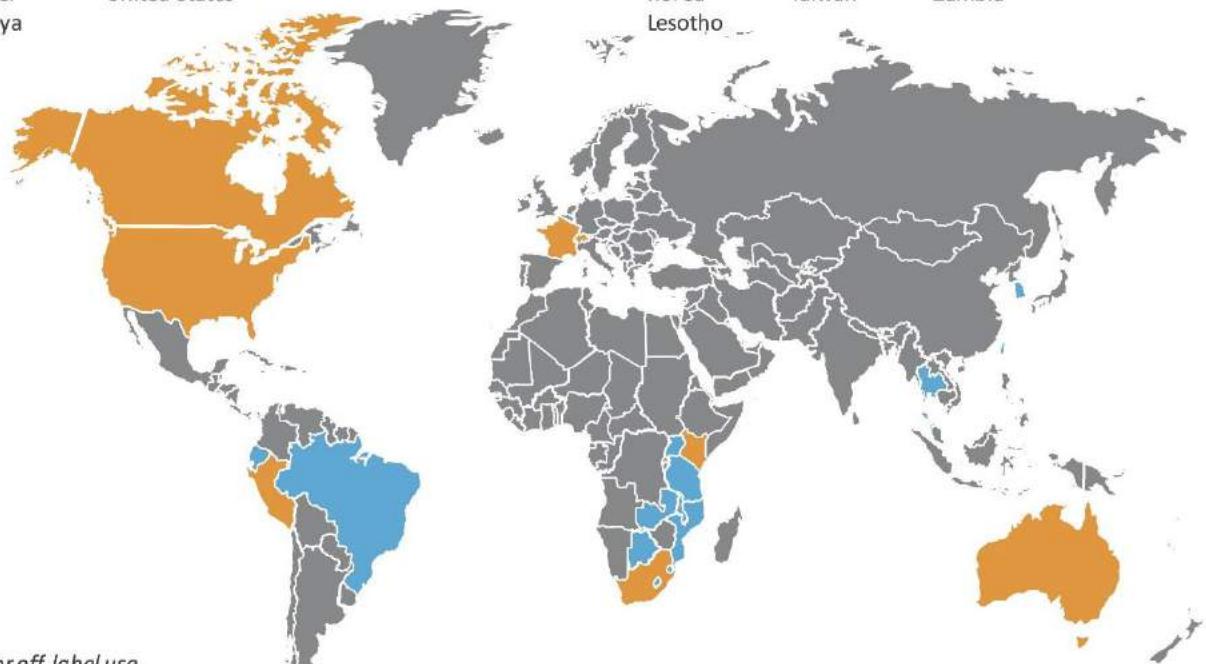
PrEP – regulatory status in 2016

Truvada approved for prevention

Australia
Canada
France
Israel
Kenya
Peru
South Africa
Switzerland ¹
United States

Regulatory application filed for a prevention indication for Truvada ^{2,3}

Botswana
Brazil
Ecuador
Korea
Lesotho
Malawi
Mozambique
Swaziland
Taiwan
Tanzania
Thailand
Uganda
Zambia



1. Approved for off-label use.

2. The European Medicines Agency (EMA) is evaluating Gilead's application for Truvada as PrEP.

3. Expected filing in Zimbabwe Q2 2016.

Updated May 2016

South Africa: PrEP programme for to sex workers launched June 2016

Oral HIV help for sex workers

LIFESTYLE / 01 Jun '16, 10:15am

 Vuyo Mkize

Johannesburg - As of Wednesday (June 1, 2016), sex workers in selected sites around the country will for the first time be able to receive oral antiretrovirals as pre-exposure prophylaxis (PrEP).









The Department of Health made this announcement in a statement on Tuesday, following Health Minister Aaron Motsoaledi's commitment in his budget speech in May that selected sex worker programmes around the country would offer PrEP in addition to other HIV preventions, and offer treatment upon diagnosis for those who are HIV-positive.



How can I prevent HIV?

**WE ARE
THE GENERATION
THAT WILL END
HIV**

TAKEN DAILY,
PrEP IS AN ADDITIONAL
PREVENTION
OPTION

-  Condoms
-  PrEP
-  Counselling
-  Post-exposure prophylaxis
-  Healthy lifestyles
-  Treatment for STIs
-  Male medical circumcision
-  ART for partners living with HIV



health

Department:
Health
REPUBLIC OF SOUTH AFRICA

ORAL PREP FOR ADOLESCENT GIRLS AND YOUNG WOMEN

PrEP in Africa - key questions for implementation

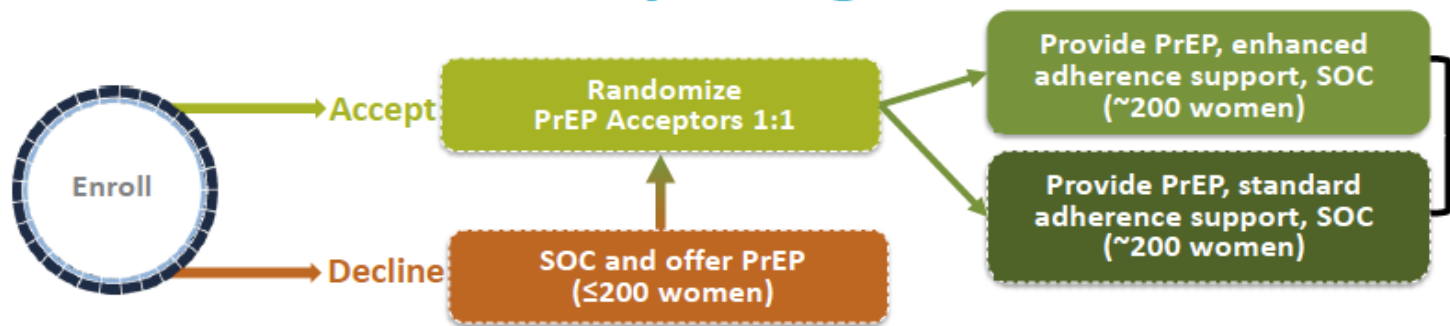
- How do you create demand?
 - What information is needed?
 - What testing services are needed?
- How do you support supply?
 - How do you identify those at highest risk without creating stigma?
 - What services are needed?
 - How do we integrate with other interventions?
- How do you support effective use?
 - What does adherence support look like?
 - Counselling, SMS, clubs
 - Drug feedback levels
 - Targeted/intensification for those who need more support?

Primary Objectives of HPTN 082

- To assess the proportion and characteristics of young HIV-uninfected women who accept versus decline PrEP at enrollment.
- To assess the difference in PrEP adherence in young women randomized to the enhanced (using drug level feedback) versus standard arms.

Study Design

PrEP = Daily oral FTC/TDF



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

Primary objectives:

- Assess the characteristics of women who accept versus decline PrEP
 - Assess PrEP adherence using drug levels in young women

HPTN 082 secondary objectives

- Timing of PrEP acceptance among women who initially decline PrEP at enrollment but elect to accept PrEP during follow up.
- Correlates of early and delayed acceptance of PrEP.
- Correlates of PrEP adherence at Weeks 13, 26, and 52.
- Proportion who discontinue PrEP, timing, & factors associated with PrEP discontinuation.
- Specificity and predictive value of a PrEP readiness tool [based on the HIV Prevention Readiness Measure (HPRM)] to predict uptake and adherence to oral PrEP.
- Qualitative factors that influence women's decisions to use PrEP, to adhere to PrEP, and acceptability of PrEP in the first 3 months after PrEP acceptance.
- Adverse events between women on PrEP and women not taking PrEP.
- HIV incidence in those who accept PrEP compared to those who do not.
 - And assess the association with detectable TFV in PrEP users who acquire HIV infection during the study.

Adherence support interventions

- Film – what is PrEP
- Counselling
 - Cognitive behavioural therapy
 - +/- feedback on drug levels at week 8, 13
- Weekly SMS
 - Hey girl, how are you?
- Adherence clubs

Film – What is PrEP

- 3 min video in which young women speak about PrEP in lay language
- Script vetted with youth CABs in Harare, Joburg, and Cape Town
- Wits RHI is leading the PrEP film development
- Filmed by youth video group with young women in Joburg & Cape Town, with some footage included from Harare

HPTN 082 counseling

- Built on tenets of cognitive-behavioral therapy
- Incorporating elements of empowerment theory
- Activities drawn primarily from youth-focused interventions have developed (e.g., ACCEPT and EVOLUTION) for young women ages 16-24
- Adaptation of AIM activity from Life Steps - used with youth in ATN 080

HPTN 082 Counseling Sessions

Session	Topics
Session 1 (Enrollment)	PrEP information 101, PrEP adherence overview, social support, introduce AIM
Session 2 (Week 4)	Adherence review, exploring motivation for PrEP adherence, safe disclosure of PrEP, use AIM
Session 3 (Week 8)	Review adherence barriers, problem solving and skill building around adherence, impact of emotions and stress on adherence
Session 4 (Week 13)	Gender dynamics, disclosure of PrEP to sexual partner, reproductive decision making, AIM
Booster Session #1 (week 26)	Reinforce adherence, transition materials
Booster Session #2 (week 39)	Reinforce adherence, transition materials

Week 4 and 8 drug level feedback plus counseling

- Half of women will be randomized to receive feedback about their 4 & 8 week drug levels
- Will use DBS results to provide view of prior 3-4 weeks adherence



6-7 doses per week
“Doing great; keep it up”



3-5 doses per week
“Doing OK”
(& problem solve barriers to adherence)



≤ 2 doses per week
“Weak signal, not enough for protection”
(& problem solve barriers to adherence)

HPTN 082 Two-way SMS

- Friendly user interface to send weekly SMS check-ins
 - Modeled after WelTel program which increased ART adherence in Kenya (Lester, Lancet 2010)
 - Provides a way to check in with young women about whether they are having any concerns with PrEP during first 12 weeks
- Transmission data will be collated to determine who & which women respond with concerns
- Will evaluate outcomes of call-backs

HPTN 082 Monthly Adherence Clubs

- Promote peer support
 - By sharing experiences and providing advice
 - Creates a cohort effect amongst ppts
- Address concerns about PrEP & adherence
 - Study staff and participants openly discuss issues
- Encourage uptake by non-users
- Encourage adherence strategies
- Formal and informal mix
 - Recreational and “educational”:
 - Sports, movies, music, drama, income generation, tutoring
 - Motivational talks
 - Involving partners / parents? (open days?)

Status of HPTN 082

- Version 1 approved Dec 2015
- IRB submissions & regulatory approvals underway
- Video & 2 way SMS development underway
- Site activation underway
- Trainings planned for July 2016
- First enrollments July 2016

HPTN 082 team



Counseling & recruitment workshop,
Joburg, May 2016

HPTN 082 acknowledgements

- Connie Celum (protocol chair)
- Protocol team, including Sybil Hosek, Bonnie Dye and Frances Cowan
- PrEP trials & demonstration project teams
- Funders: NIH, BMGF, USAID

ACKNOWLEDGEMENTS

The HIV Prevention Trials Network is sponsored by the National Institute of Allergy and Infectious Diseases, the National Institute of Mental Health, and the National Institute on Drug Abuse, all components of the U.S. National Institutes of Health.

Wanted: Biomedical prevention options for women



Ongoing work may define new products, including vaginal rings (in phase III), long-acting injectables (in phase II), and other options.

Oral pills for PrEP can be thought of as a 1st generation product.

New products should fill gaps in patient preferences and provide choice of methods

Key is to not always look to unproven new technologies and miss the successes that we can grasp now.

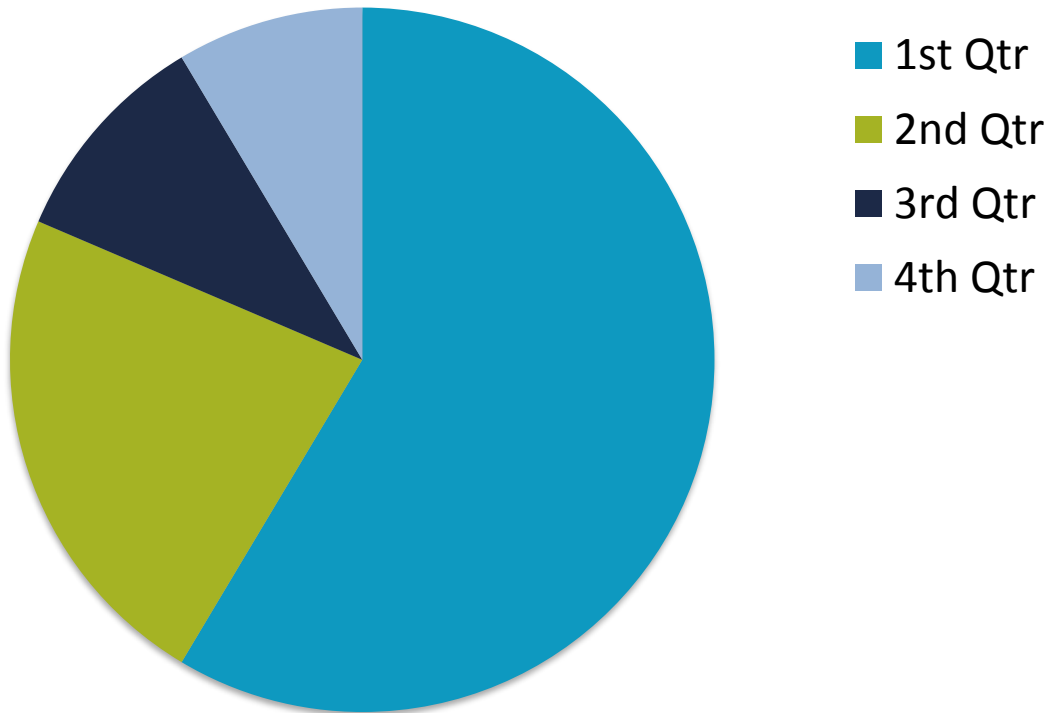
Summary

- What are the key takeaways
 - Summarize each point
 - Be concise

SAMPLE GRAPHIC SLIDE

DON'T JUST TELL THEM. SHOW THEM.

Sample



Sample Style

- Sample text for bullet
 - The secondary bullet looks like this
 - And there are a few more levels
- And another bullet here

