Pre-Exposure Prophylaxis (PrEP): New options to Prevent HIV and end the epidemic

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DISCLOSURES

- No conflict of interest
- Some slides have been sourced from publicly available presentations online

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LEARNING OBJECTIVES

After attending this presentation, learners will be able to:

- Understand what PrEP is
- Understand how it prevents HIV
- Understand what is needed to start PrEP

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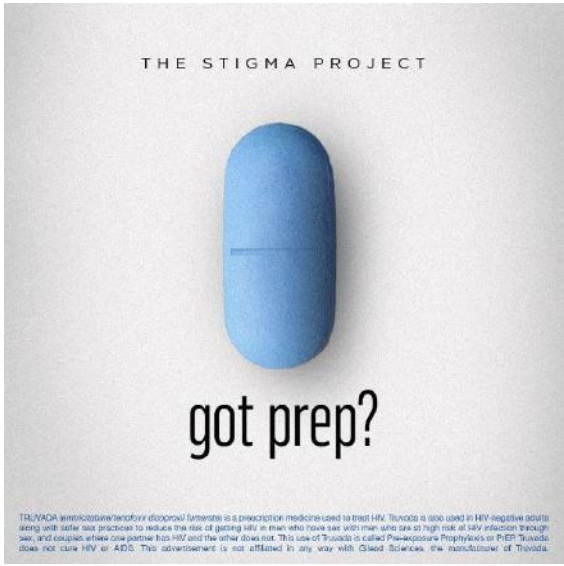
Pre-Exposure Prophylaxis (PrEP)

PrEP is the use of ARV drugs by HIV-uninfected persons to prevent the acquisition of HIV before exposure to HIV.

Pre	• Before
Exposure	• Activity that can lead to HIV infection
Prophylaxis	• Prevention

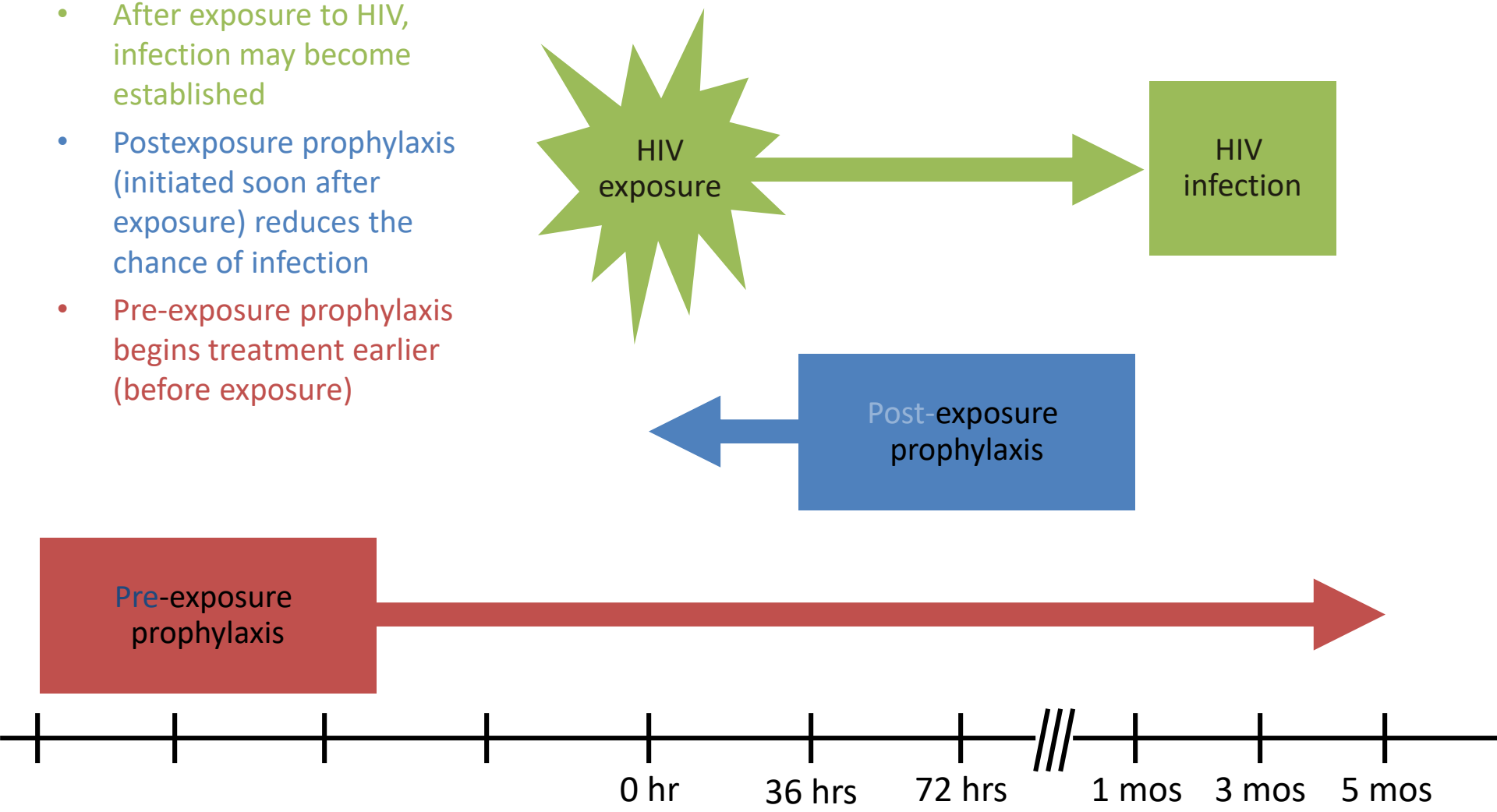
What is PrEP?

- Tenofovir/emtricitabine currently
- Why tenofovir/emtricitabine for PrEP?
  - Efficacy shown in clinical studies
  - One pill, once a day
  - Favorable safety and tolerability profiles



Pre- vs Post-exposure Prophylaxis

- After exposure to HIV, infection may become established
- Postexposure prophylaxis (initiated soon after exposure) reduces the chance of infection
- Pre-exposure prophylaxis begins treatment earlier (before exposure)



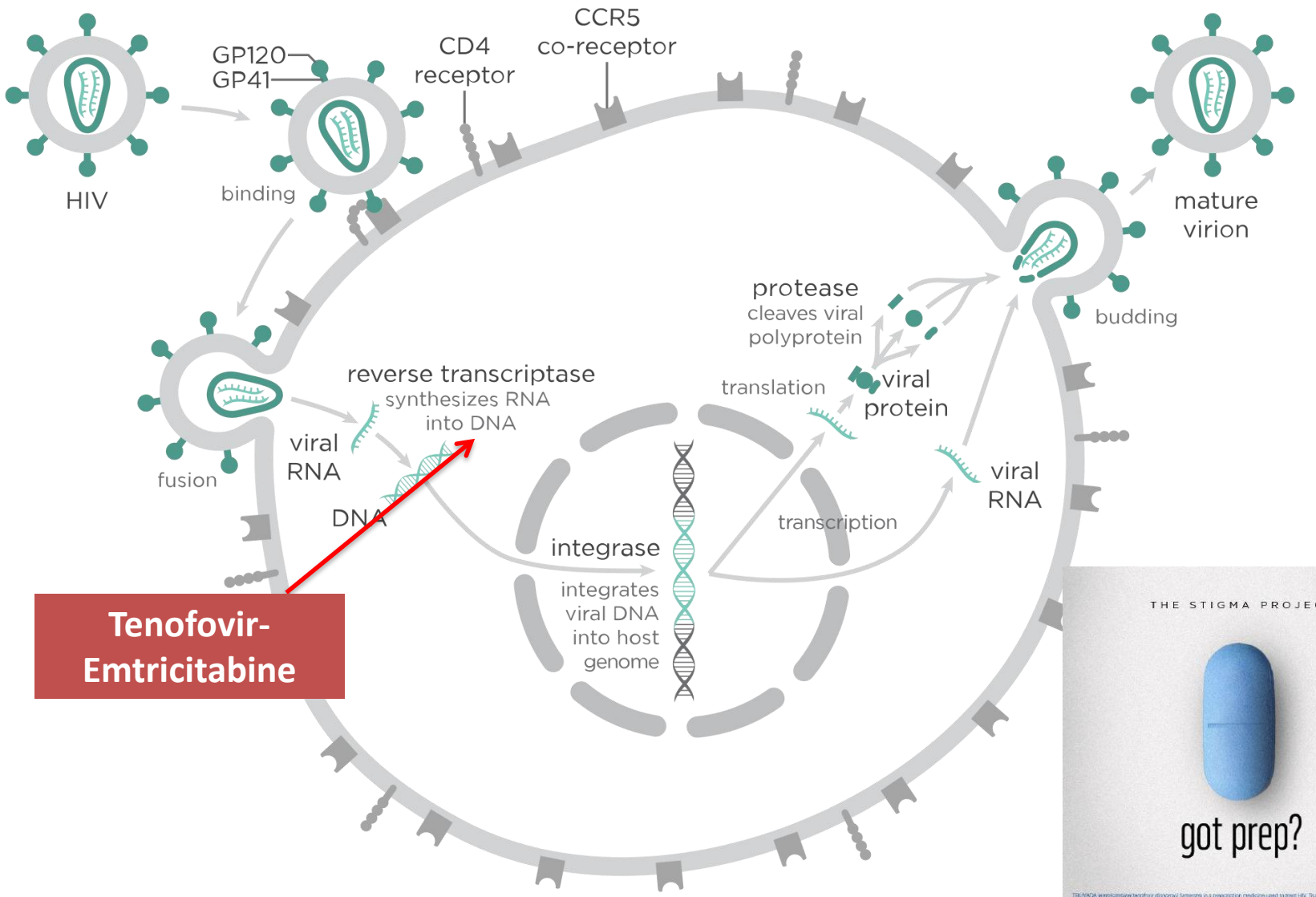
Courtesy: Carlos Malvestutto, Nationwide Children's Hospital, Ohio State University Medical Center

What is PrEP?

- Pre-Exposure Prophylaxis is a new HIV prevention method in which an HIV-uninfected individual takes antiretroviral medication ***before*** a potential HIV exposure to prevent infection.
- Does this idea of PrEP sound familiar?

Women take birth control pills prior to intercourse to prevent pregnancy

How does PrEP with Tenoforvir-Emtricitabine work?



The NEW ENGLAND JOURNAL of MEDICINE

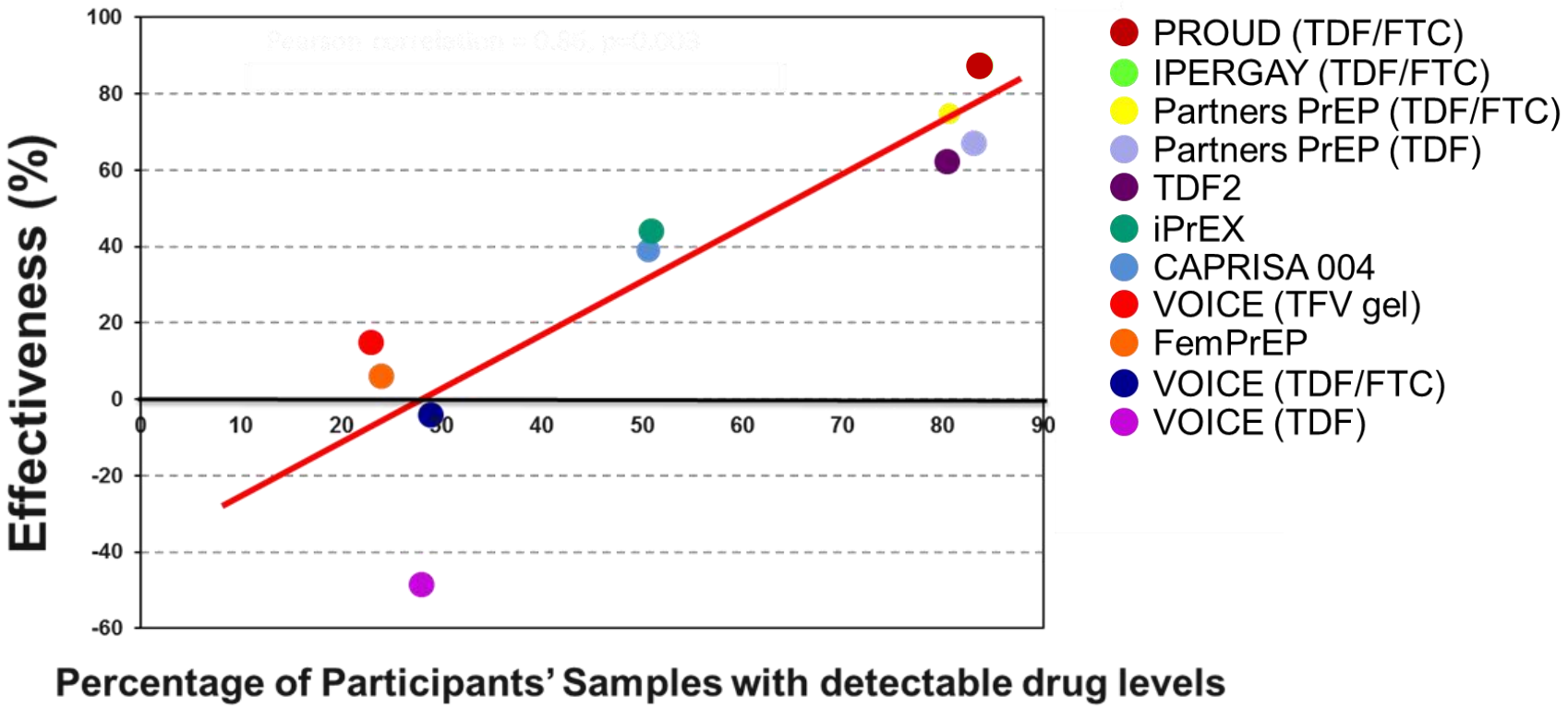
ESTABLISHED IN 1812 DECEMBER 30, 2010 VOL. 363 NO. 27

Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

Robert M. Grant, M.D., M.P.H., Javier R. Lama, M.D., M.P.H., Peter L. Anderson, Pharm.D., Vanessa McMahan, B.S., Albert Y. Liu, M.D., M.P.H., Lorena Vargas, Pedro Goicochea, M.Sc., Martín Casapía, M.D., M.P.H., Juan Vicente Guanira-Carranza, M.D., M.P.H., Maria E. Ramirez-Cardich, M.D., Orlando Montoya-Herrera, M.Sc., Telmo Fernández, M.D., Valdilea G. Veloso, M.D., Ph.D., Susan P. Buchbinder, M.D., Suwat Chariyalertsak, M.D., Dr.P.H., Mauro Schechter, M.D., Ph.D., Linda-Gail Bekker, M.B., Ch.B., Ph.D., Kenneth H. Mayer, M.D., Esper Georges Kallás, M.D., Ph.D., K. Rivet Amico, Ph.D., Kathleen Mulligan, Ph.D., Lane R. Bushman, B.Chem., Robert J. Hance, A.A., Carmela Ganoza, M.D., Patricia Defechereux, Ph.D., Brian Postle, B.S., Furong Wang, M.D., J. Jeff McConnell, M.A., Jia-Hua Zheng, Ph.D., Jeanny Lee, B.S., James F. Rooney, M.D., Howard S. Jaffe, M.D., Ana I. Martinez, R.Ph., David N. Burns, M.D., M.P.H., and David V. Glidden, Ph.D., for the iPrEx Study Team*

Effectiveness of Daily TDF/FTC in Clinical Trials

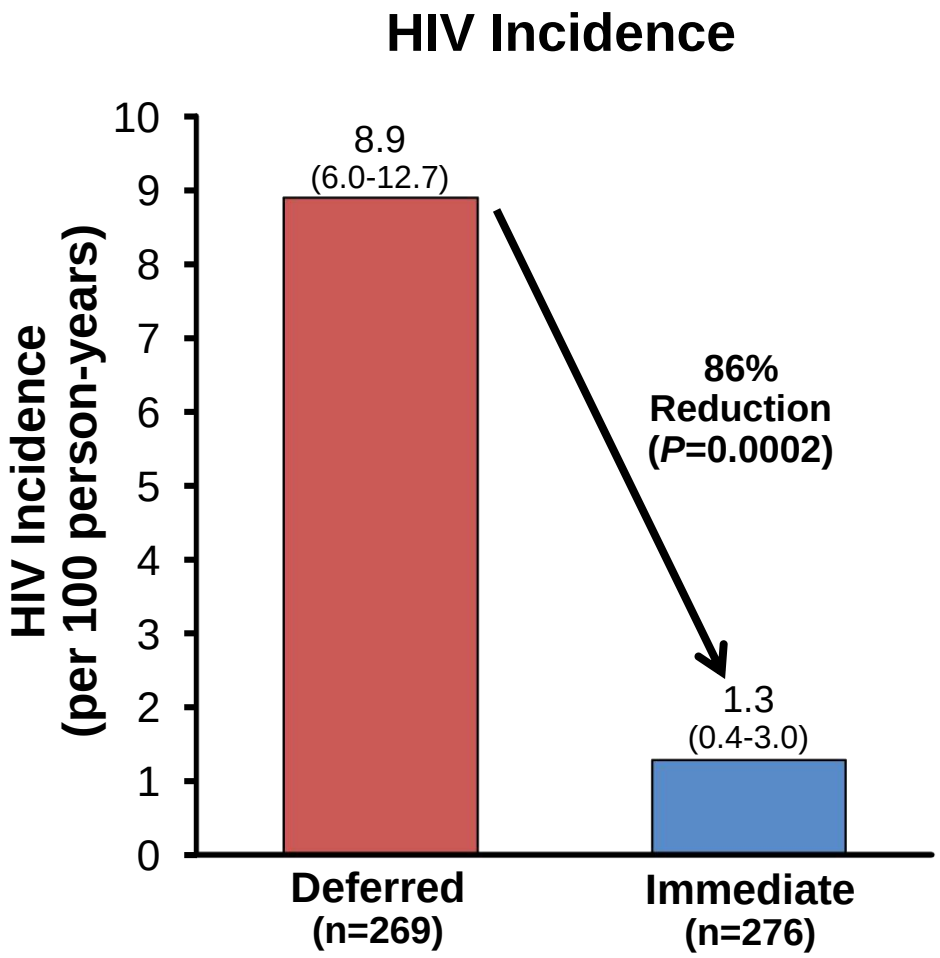
PrEP is very Effective



SS Abdool Karim, personal communication

Real world PrEP: PROUD Study

- ↓ new HIV infections with immediate versus deferred PrEP (3 versus 20 cases)
  - 86% reduction (*P*=0.0002)
- Incident HIV infection in the immediate group
  - HIV infection predated start of ART (n=1)
  - No drug/not adherent (n=2)
- Number needed to treat to prevent 1 HIV infection: 13



McCormack S, et al. *Lancet*. 2016;387:53-60.

Oral PrEP containing TDF

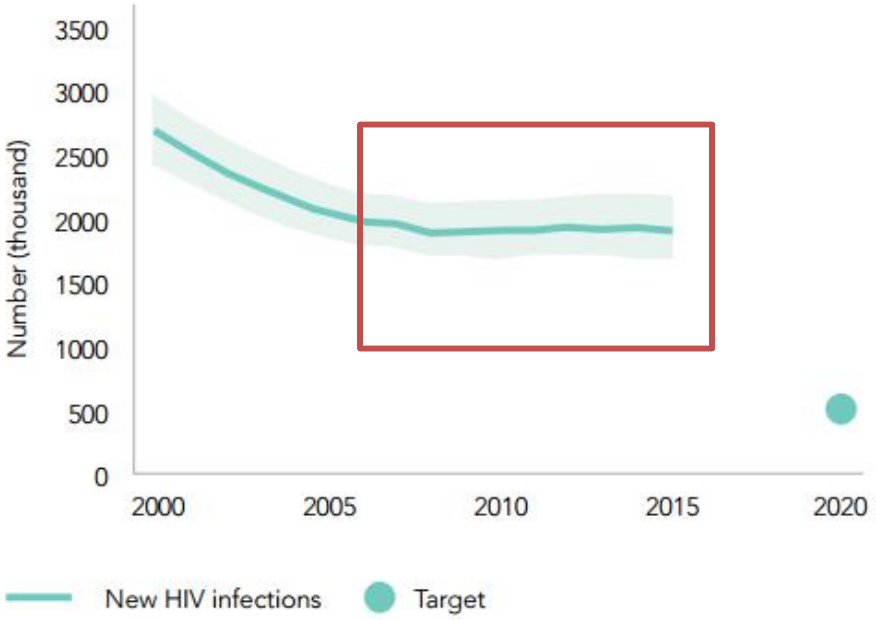
Recommended for any person at substantial HIV risk

(as part of combination prevention)

- WHO strong recommendation, high quality evidence (2016 WHO consolidated ARV guidelines update)
  - Systematic review and meta-analysis of clinical research (Fonner et al, *AIDS*, 2016)
  - Adherence is the critical predictor
- Essential Medicines List (EML) recently added PrEP medicines (2017)
- For MSM-TG everywhere, SWs in most settings (given epidemiology), other populations (e.g. adolescent girls and young women)

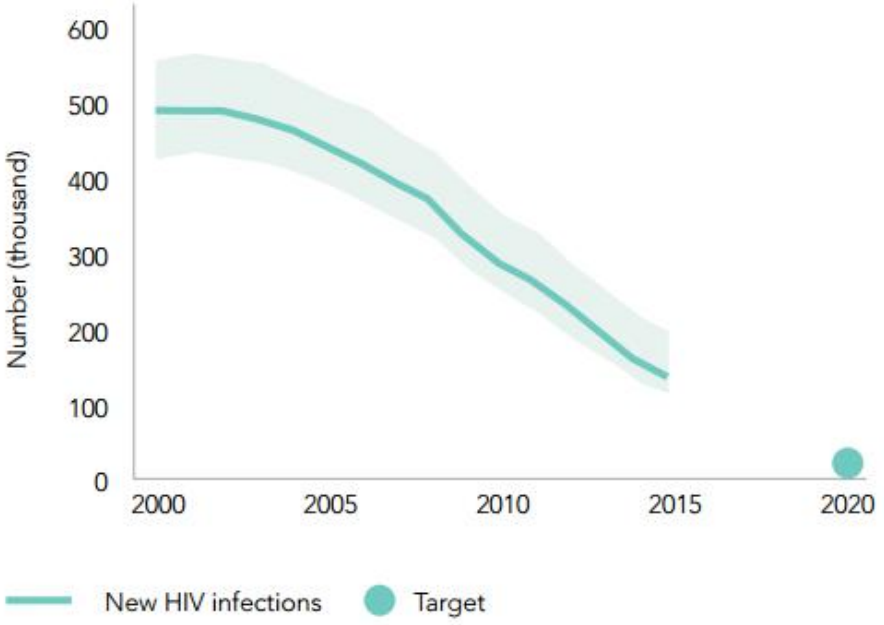
Global HIV transmission PERSISTS:
Treatment scale-up has 'masked stagnation in the estimated annual number of new HIV infections' (Baggaley et al, *JIAS*, 2016)

New HIV infections among adults (aged 15 years and older), global, 2000–2015



Source: UNAIDS 2016 estimates.

New HIV infections among children (aged 0–14 years), global, 2000–2015



Source: UNAIDS 2016 estimates.

Prevention Gap Report (UNAIDS), 2016: http://www.unaids.org/sites/default/files/media_asset/2016-prevention-gap-report_en.pdf

Why We Need PrEP

- HIV transmission continues
- New approaches to combination HIV prevention are needed

- PrEP is a promising new intervention for people at substantial risk for HIV
- PrEP has been widely studied

- PrEP is highly effective and safe
- PrEP can be cost-effective

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Condoms and Lube

- Condoms (both insertive and receptive) work if used correctly and consistently
  - Also estimated to reduce risk of syphilis infection by about 50% to 66%
- An option that works for some individuals, but not on a population level
  - CDC data: majority of men who have sex with men have had sex without a condom at least once in the past year with a partner of unknown HIV status
  - One night stand: the protective benefits do not translate to future sexual acts

Why We Need PrEP

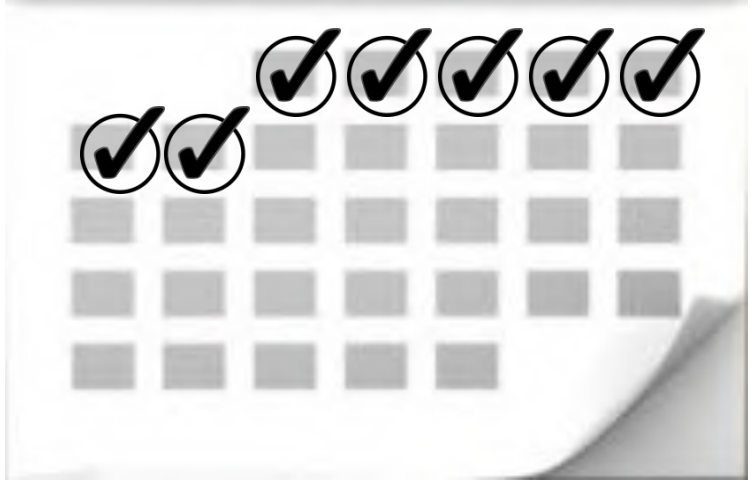
- Several effective HIV prevention interventions already exist, including condoms and harm reduction for people who inject drugs (PWID).
- Global annual HIV infections have remained consistently close to 2 million for several years, declining in recent years.
- HIV incidence remains high among key and vulnerable populations: PWID, sex workers (SWs), transgender persons (TG), men who have sex with men (MSM).
- PrEP provides an *additional* prevention intervention to be used *together* with existing interventions like condoms.
- PrEP is not meant to replace or be a substitute for existing prevention interventions.

More Than PEP and PrEPs

- Lesson from contraception: human beings need options
- PrEP isn't just about stopping HIV acquisition:
  - Mental health: peace of mind, reduction of fear
  - Anti-stigma: PrEP helps HIV-negative people see the human and not the HIV
  - Possibility for increased sexual intimacy
- PEP isn't just another option for stopping an infection:
  - Imagine you believe you've been exposed to HIV and you're not on PrEP: PEP is your last prevention option
  - Every time that someone can't access PEP after a possible exposure is an inexcusable injustice and major societal failure

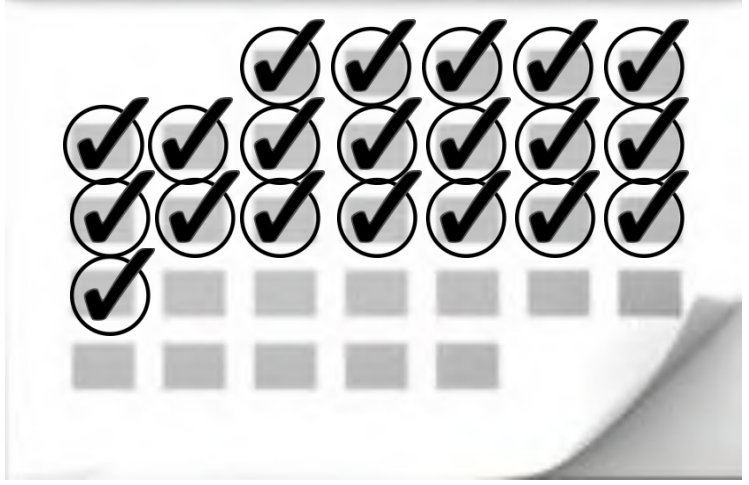
Time to protection

Rectal Transmission



7 days

Vaginal Transmission



20 days

Who is PrEP for?

PrEP is for all people at substantial risk of HIV infection. PrEP can be particularly beneficial for people who are unable to use other HIV prevention methods, for example people who struggle using condoms or have barriers to condom use.

Rwanda Guidelines:

- Sero-different couples with detectable viral load
- Men who have sex with men (MSM)
- Sex Workers

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Eligibility for PrEP

Eligibility criteria include:

- HIV seronegative
- No suspicion of acute HIV infection
- At substantial risk* of HIV infection
- Creatinine clearance (eGFR) >60ml/min**
- Willingness to use PrEP as prescribed

* Defined below

** eGFR: estimated glomerular filtration rate. Waiting for creatinine result should not delay initiation of PrEP

Risk for HIV infection
(based on history in the past six months)

- **Client who is sexually active in a high HIV prevalence population (either in the general population or key population group) PLUS reports *ANY* of the following in the past six months**:
  - Vaginal or anal intercourse without condoms with more than one partner, OR
  - Sex partner with one or more HIV risk, OR
  - History of an STI (based on lab test, syndromic STI treatment, self-report), OR
  - History of use of post-exposure prophylaxis (PEP)

OR

- **Client who reports history of sharing of injection material/equipment with another person in the past six months.**

OR

- **Client who reports having a sexual partner in the past six months* who is HIV positive *AND* who has not been on effective HIV treatment.**

  **On ART for less than six months, or has inconsistent or unknown adherence*

Eligibility with Baseline Testing

1. HIV: status check within 1 week of starting of PrEP
2. Renal: check creatinine clearance
3. Hep B: check Hep B serologies

4. Sexually transmitted infections:
   - oral, genital, rectal chlamydia/gonorrhea
   - RPR (Syphilis)
5. Pregnancy testing (PrEP is SAFE in Pregnancy

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Initial PrEP Visit:

Investigation	Rationale
HIV test	• Assessment of HIV infection status • Symptom checklist for possible acute HIV infection
Serum creatinine	• To identify pre-existing renal impairment
Hepatitis B surface antigen (HBsAg)	• To identify undiagnosed hepatitis B (HBV) infection
RPR / STI screening	• To diagnose and treat STI • Syndromic or diagnostic STI testing, depending on local guidelines
Pregnancy testing	• To ascertain pregnancy

Prescribing PrEP

- Tenofovir/emtricitabine 300/200mg, 1 tablet by mouth daily

- **Common side effects**
  - Nausea, flatulence, headache
  - Contraindicated if creatinine clearance < 60
- Less common ***reversible*** adverse effects
  - Acute kidney injury
  - Long term use can lead to decreases in bone mineral density ~1%, BUT is reversible

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PrEP is Safe

- Side effects are mild and usually temporary

- **Common side effects**
  - Nausea, flatulence, headache
  - Contraindicated if creatinine clearance < 60

- Less common ***reversible*** adverse effects
  - Acute kidney injury (1 in 200, but mostly in over 40-50yo)
  - Long term use can lead to decreases in bone mineral density ~1%,

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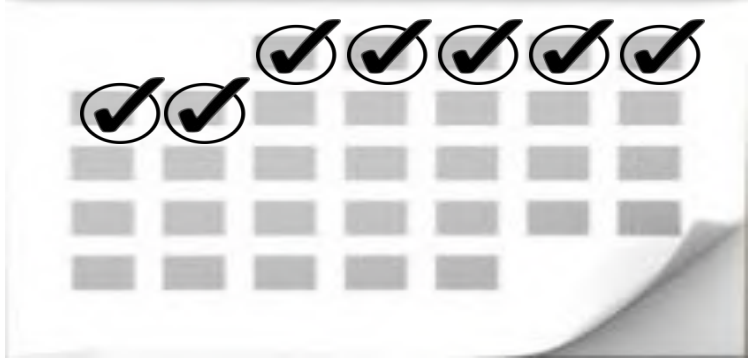
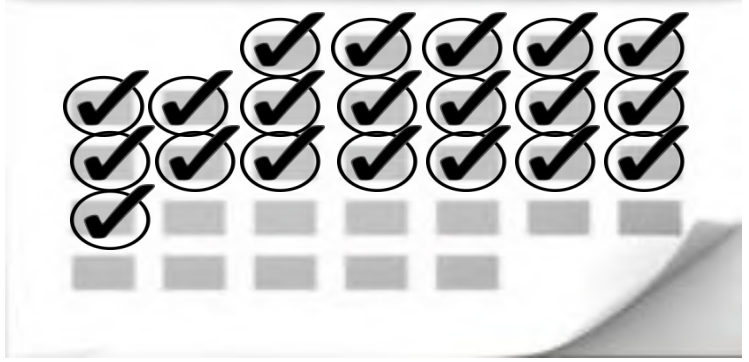
Time to protection

Rectal Transmission



7 days

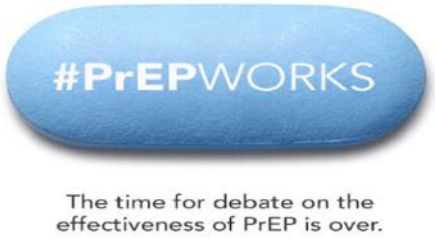
Vaginal Transmission



20 days

Discontinuation of PrEP

- Personal choice
- Changed life situations – **Risk for HIV is not constant – Changes over time for most people**
- Intolerable toxicity
- Chronic non-adherence despite efforts to improve adherence
- HIV seroconversion



Key Initial Visit Counselling Messaging: PrEP Efficacy

PrEP works when taken!

PrEP reaches maximum effectiveness after seven daily doses.

PrEP does not prevent most sexually transmitted infections other than HIV. Condoms used with every act of sexual intercourse provides some protection against many of these infections.

PrEP does not prevent pregnancy. Use effective contraception unless you want pregnancy.

PrEP is safe.

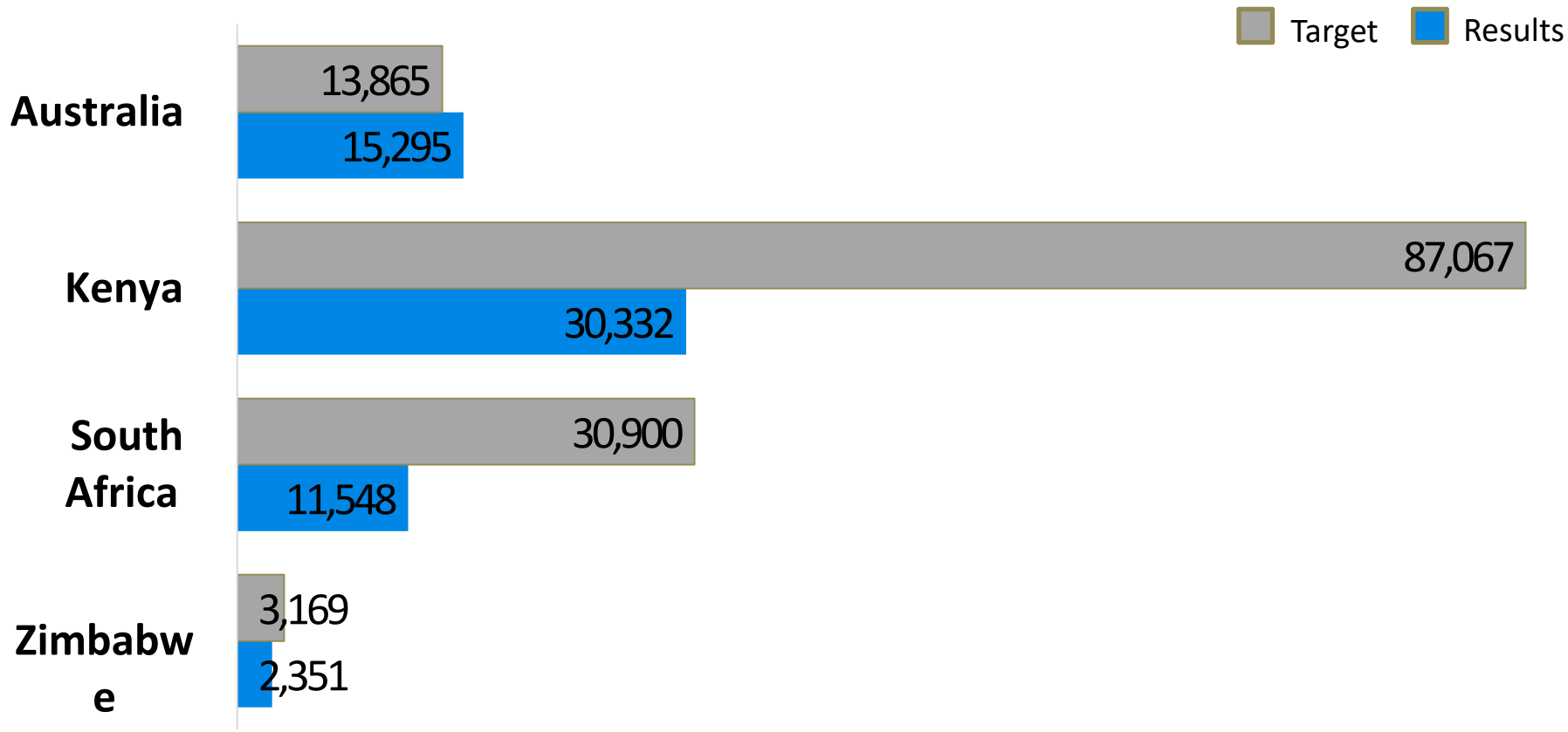
Planned, Ongoing and Completed PrEP Evaluation Studies (June 2015)

KEY Ongoing Planned Completed

For the latest on these studies, visit *www.avac.org/prep/track-research.*

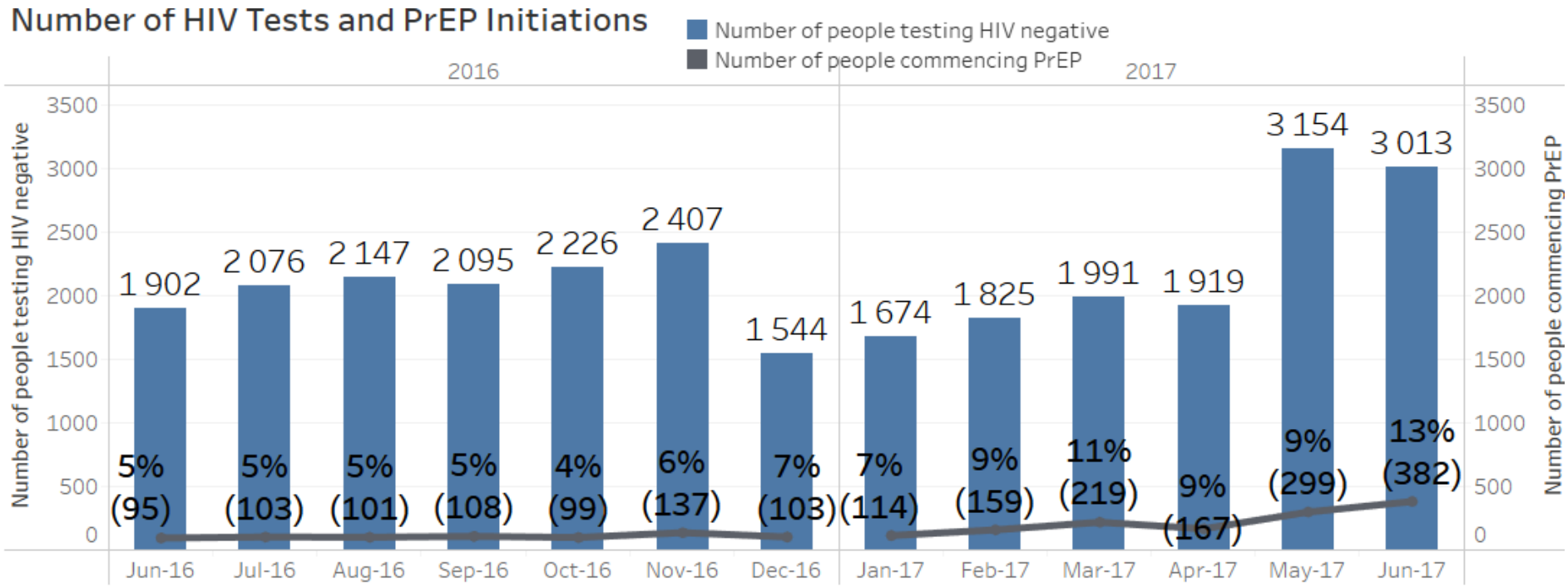
Data from demonstration projects and open-label extension studies are beginning to come in. So far, the findings suggest that people want and will take daily oral PrEP correctly outside of a clinical trial setting. Expanded and faster rollout is key.

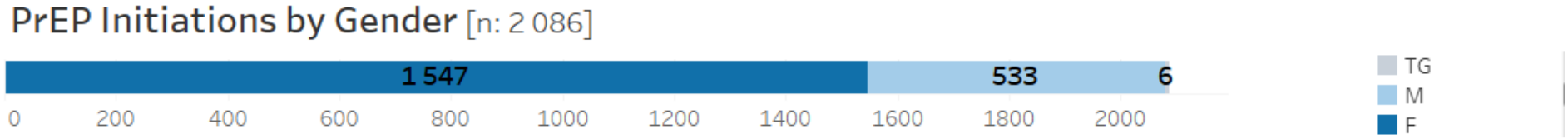
Oral PrEP Implementation: Progress Against Targets 2018*

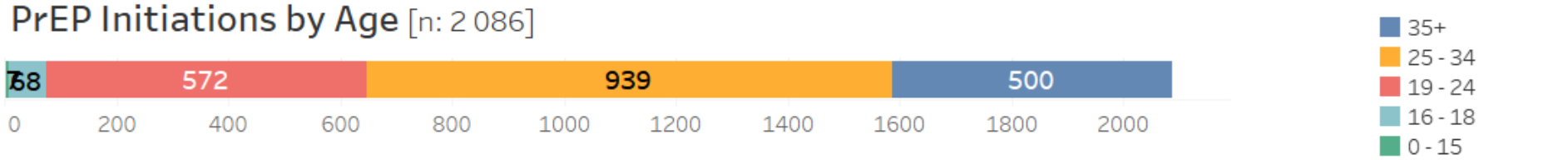


**Includes initiation and target data from ongoing demonstration and implementation projects, PEPFAR*

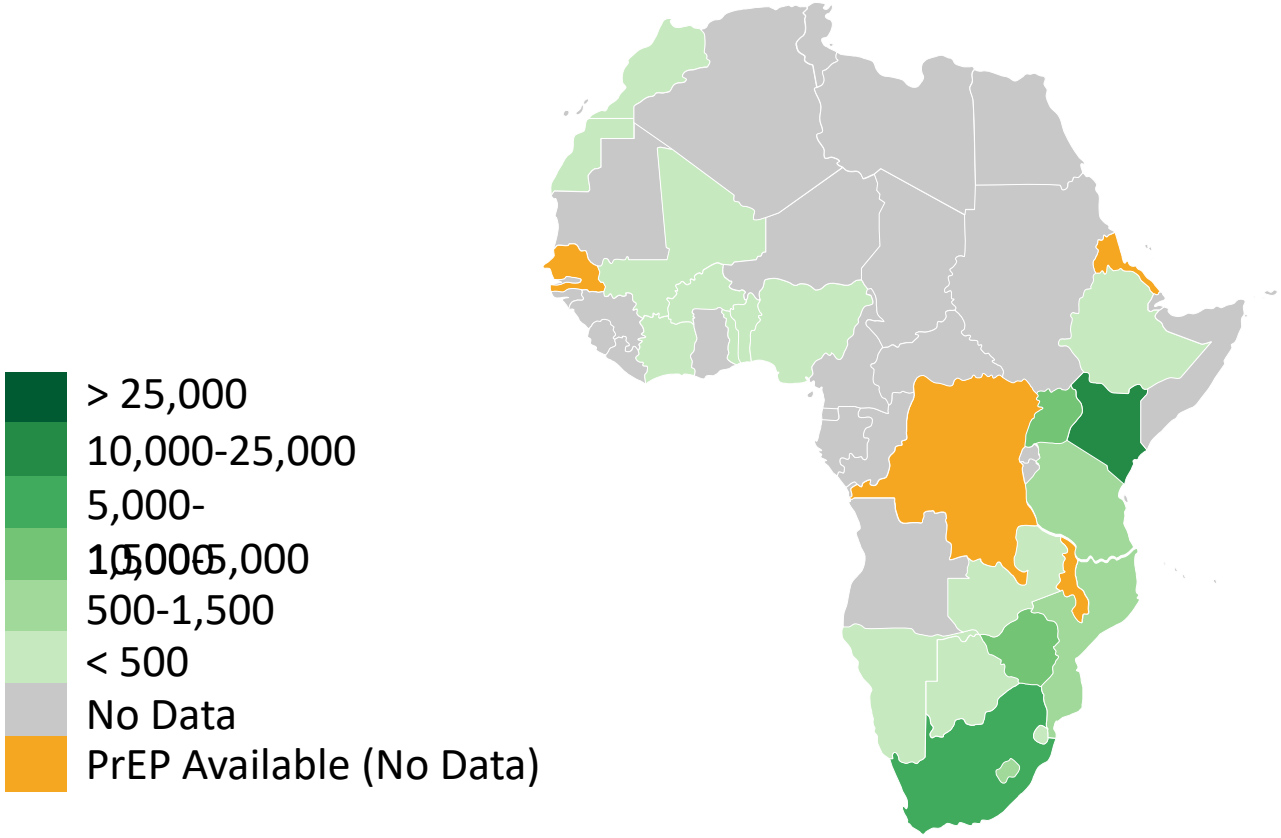
South African National PrEP roll-out







PrEP Initiations by Country (April 2018)



Source: AVAC Global PrEP Initiation Tracker 2018

New types of PrEP being studied:

Yearly Implant

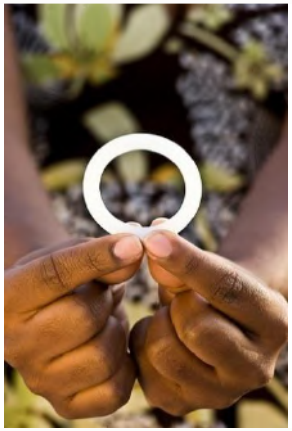
Novel adherence strategies

Hard-to-reach populations; PWUD

Alternative delivery systems and formulations

Monthly Pill

Vaginal & Rectal Microbicides (MTN 017)



Intravaginal rings (Dapivirine, +/- Contraception)

Injectables: ARVs and mAbs (Cabotegravir, VRC01)

THANK YOU FOR LISTENING

Extra Slides

Will PrEP Users Engage in More Risk Behaviors?

Will PrEP Encourage People to Use Condoms Less Often or to Have More Sexual Partners (i.e., "Risk Compensation")?

- There was *no* evidence of this in clinical trials, where participants received regular counseling, screening, and access to condoms and lubricants.
- Evidence from real-world PrEP implementation shows declines in self-reported condom use and increases in STI diagnoses among some PrEP users.
- Combination prevention should include quality counseling and access to condoms and lubricants.

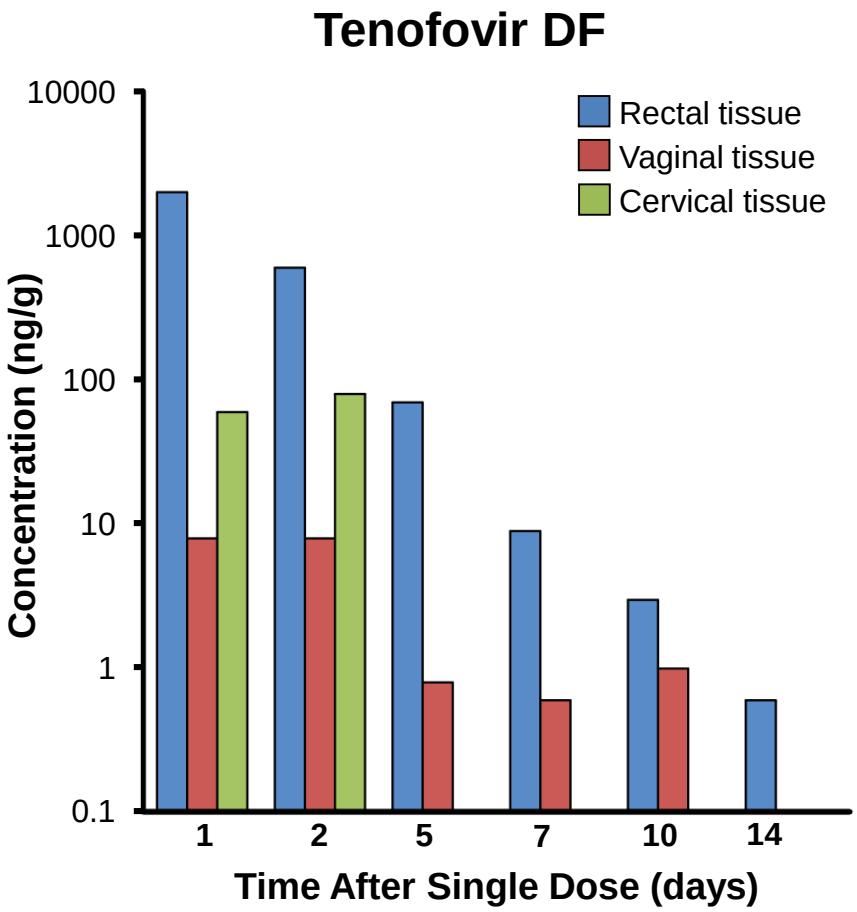
Will PrEP Lead to More HIV Drug Resistance?

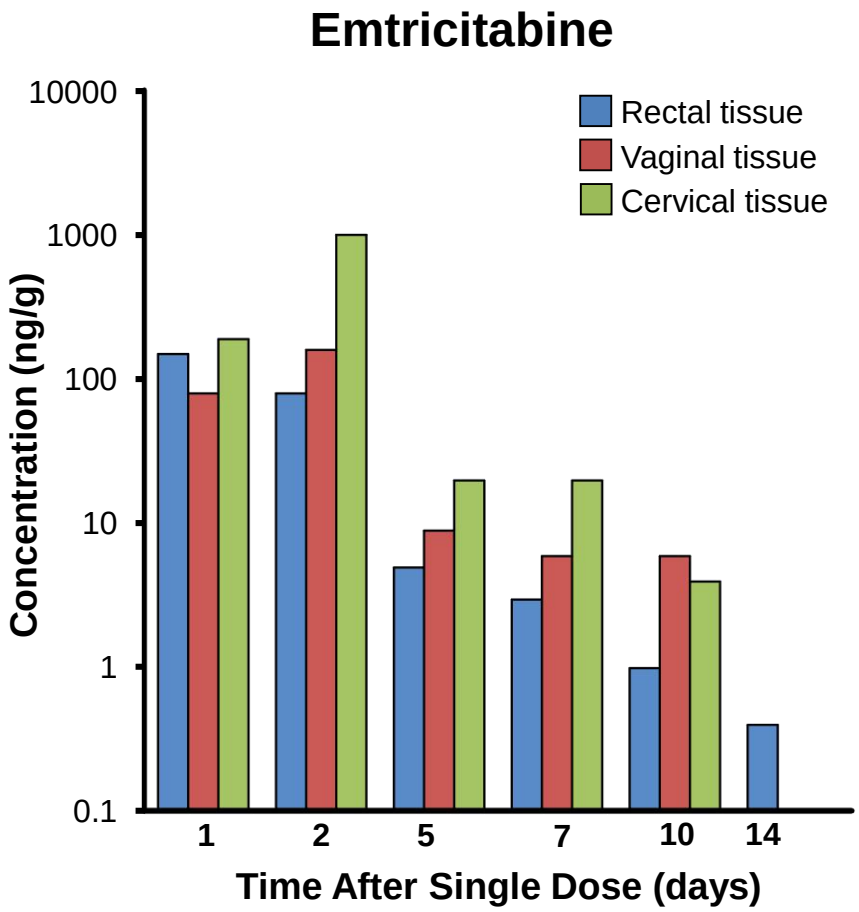
- Drug resistance (HIVDR) in PrEP users was **rare in clinical trials**.
- HIVDR occurred mostly in cases where the person had **undiagnosed HIV infection when starting PrEP**.
- HIVDR **will not occur when adherence to PrEP is high** and HIV seroconversion does not occur.
- There can be **risk of HIVDR if adherence is suboptimal** and HIV infection occurs while the individual is on PrEP.
- Optimal **PrEP adherence is crucial**.
- **Health providers must support and monitor adherence** and teach PrEP users to recognize signs and symptoms of AHI.

PrEP use During Pregnancy

- TDF appears to be safe in pregnant women, however, evidence comes from studies of HIV infected women on ART.
- Among HIV uninfected pregnant women, evidence of TDF safety comes from studies of hepatitis B (HBV) mono-infected women.
- PrEP benefits for women at high risk of HIV acquisition appear to outweigh any risks observed to date.
- WHO recommends continuing PrEP during pregnancy and breastfeeding for women at substantial risk of HIV.
  - There is however a need for continued surveillance for this population group.

PrEP and women : Varying Concentrations in Mucosal Tissues



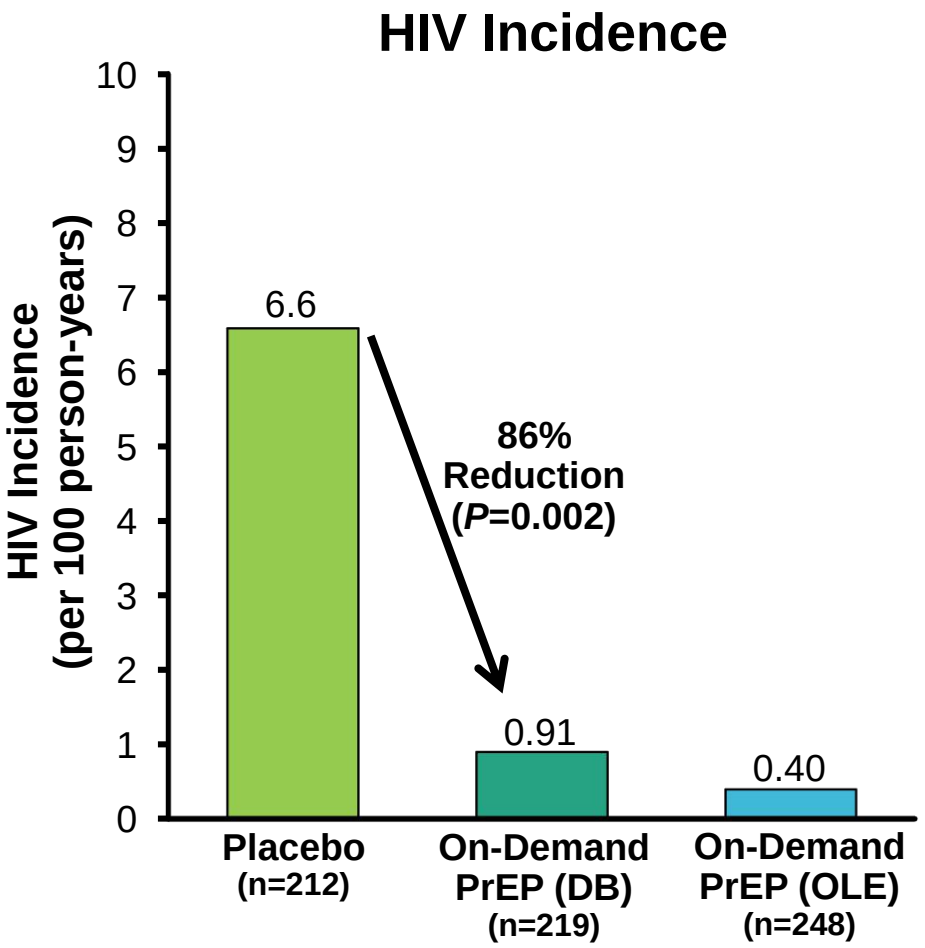


Open-label, 14-day pharmacokinetic study in HIV-negative female (n=7) and male (n=8) volunteers.
Entry criteria included: 18-50 years of age; BMI 18-30 kg/m^2; weight $\geq$50 kg; no HCV or HBV; nonpregnant women who were premenopausal and had regular menstrual cycles.

Patterson KB, et al. *Sci Transl Med.* 2011;3:112re4.

Ipergay Trial: Event-Driven PrEP

- On-demand PrEP remained highly effective
  - 1 new HIV infection during OLE
    - 1.3 months in OLE, no detectable drug since entering OLE
    - No RT resistant mutations
- New STIs during OLE (33%)
- Generally well tolerated
  - Drug-related GI AEs (10%)
- Sexual behavior
  - No significant difference compared with double-blind phase
- 1 SC in OLE, not on drug, with final data: incidence 0.19%



Molina J-M, et al. 23rd CROI. Boston, 2016. Abstract 886