

Understanding PrEP Effectiveness

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HPTN/FHI 360

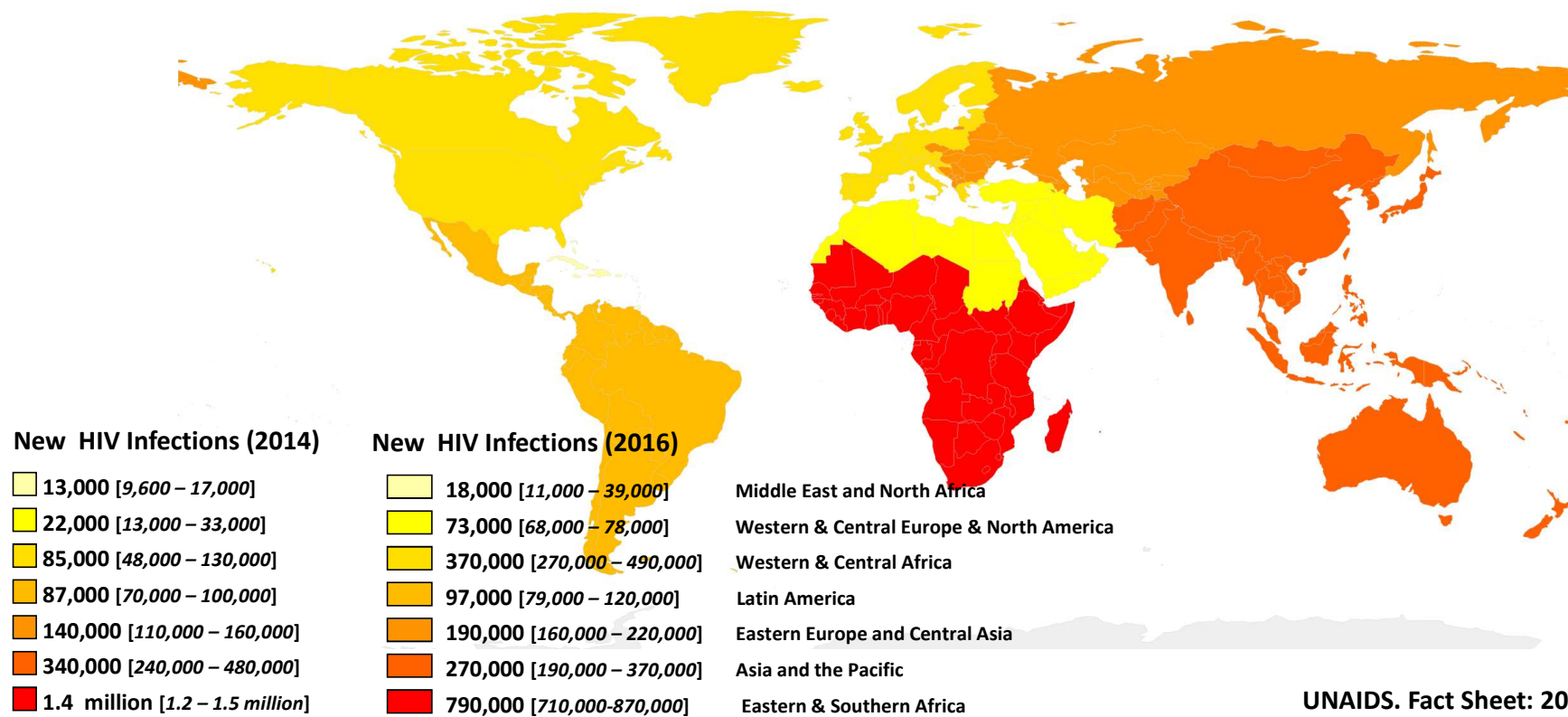
HPTN Community Working Group Meeting

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Outline

- Prevention Modalities for HIV
- PrEP
- Efficacy vs Effectiveness
- Effectiveness of TDF/FTC as PrEP
- Factors contributing to Effectiveness

1.8 Million New Infections in 2016



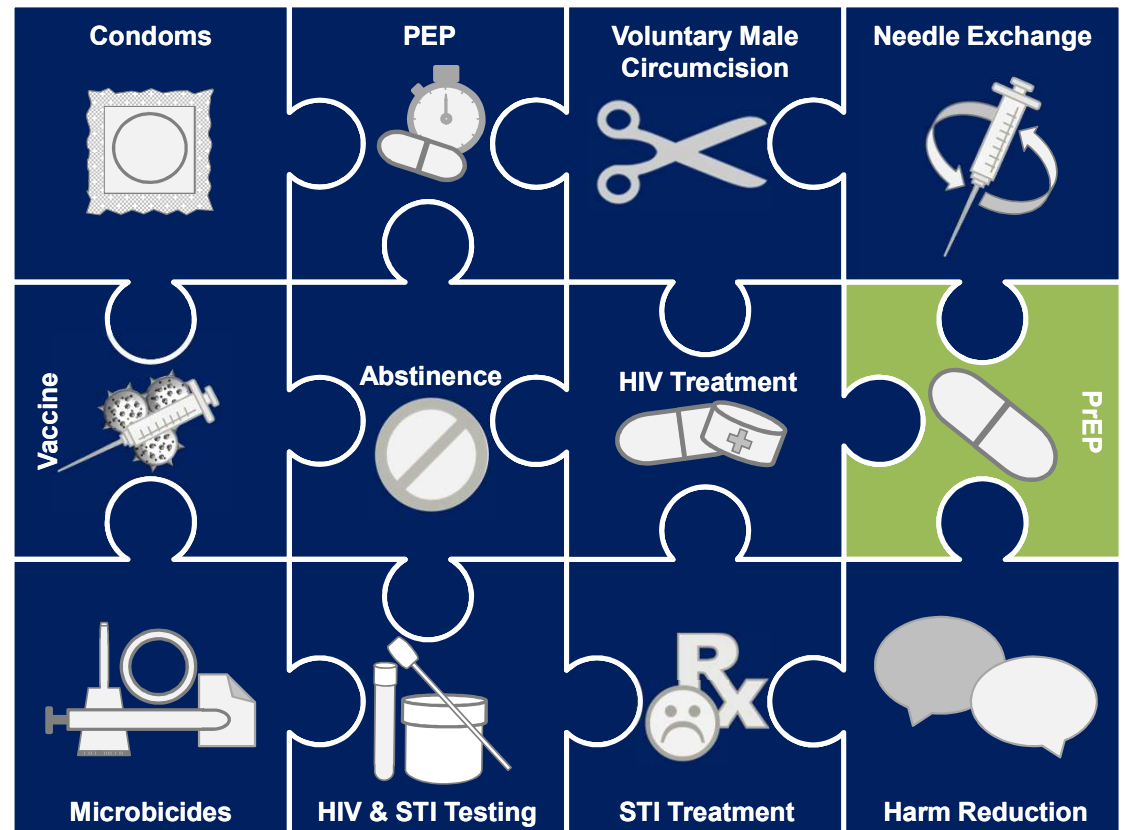
UNAIDS. Fact Sheet: 2016 Statistics; 2017.

HIV Prevention



- There are various “tools” that can prevent HIV acquisition
- New “tools” to prevent getting HIV are urgently needed

Prevention Modalities



What is PrEP?

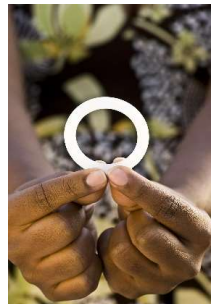
- Taking drugs before exposure to an infectious agent is called Pre-Exposure Prophylaxis
- It is a concept. A drug or combination of drugs can be used for PrEP but concept of PrEP not limited to a drug.
- Not a new concept, for example Malaria prophylaxis common for travelers is also PrEP for Malaria

Why Antiretroviral Drugs for HIV PrEP?

- Data suggesting that ARV prophylaxis may be effective
 - ARVs for PMTCT
 - Post-exposure prophylaxis for HIV (PEP)
 - Monkey models for SHIV transmission
- Available ARVs appear safe
- In 2012 the FDA approved Truvada[®] to be used as PrEP in the US for HIV prevention
- Used as part of a HIV prevention package (risk reduction counseling and condoms)

Other Candidates for PrEP

- Other drugs are being evaluated as PrEP agents: e.g. Injectable Cabotegravir, Dapivirine rings etc.
- SO Truvada is one option for PrEP, and we hope not the only option.
- SO we have to start understanding that PrEP and Truvada are not interchangeable. PrEP is a concept, Truvada is one type of PrEP
- Similar to Xerox is not the only photocopier OR Fedex is not the only courier



Efficacy and Effectiveness

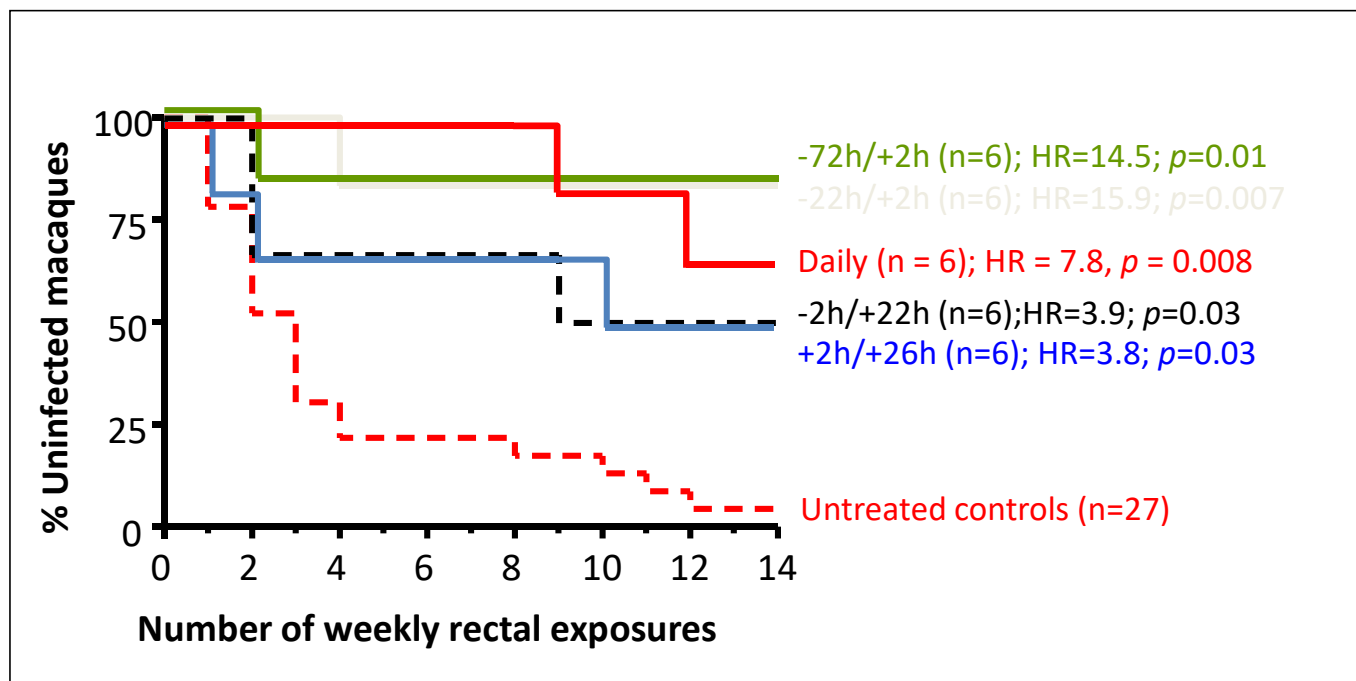
- Efficacy is the effect in perfect conditions: maximum possible effect of drug
- Effectiveness is the effect in the real world: A useful clinical effect

Example

Efficacy: *Antibiotics kill bacteria and are efficacious in curing infections.*

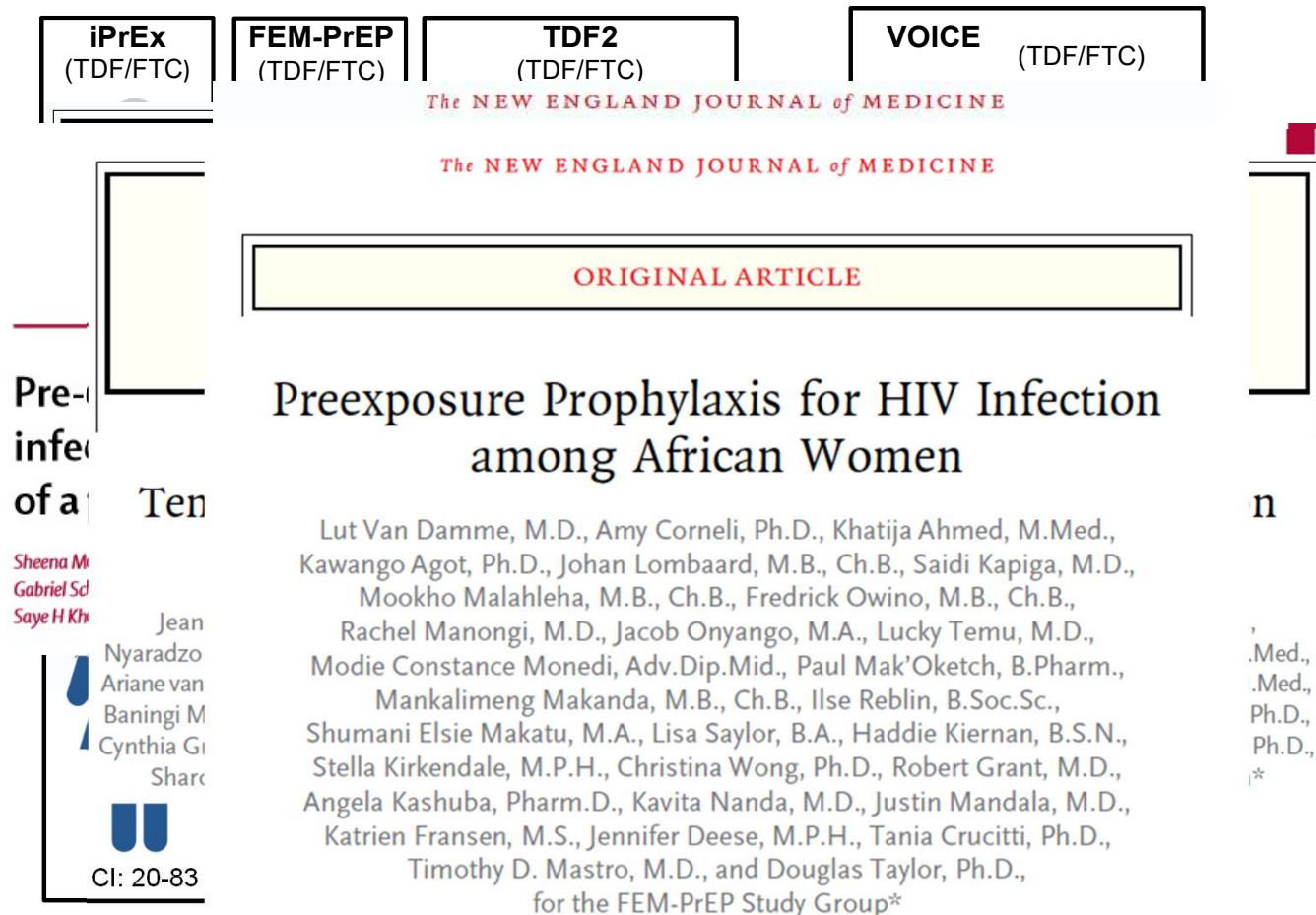
Effectiveness: *If you do not take the pills as prescribed, infection may not get cured, and may lead to a 'rebound' of those strains not killed (resistant microbes).*

Efficacy of Daily/iPrEP with Oral Truvada

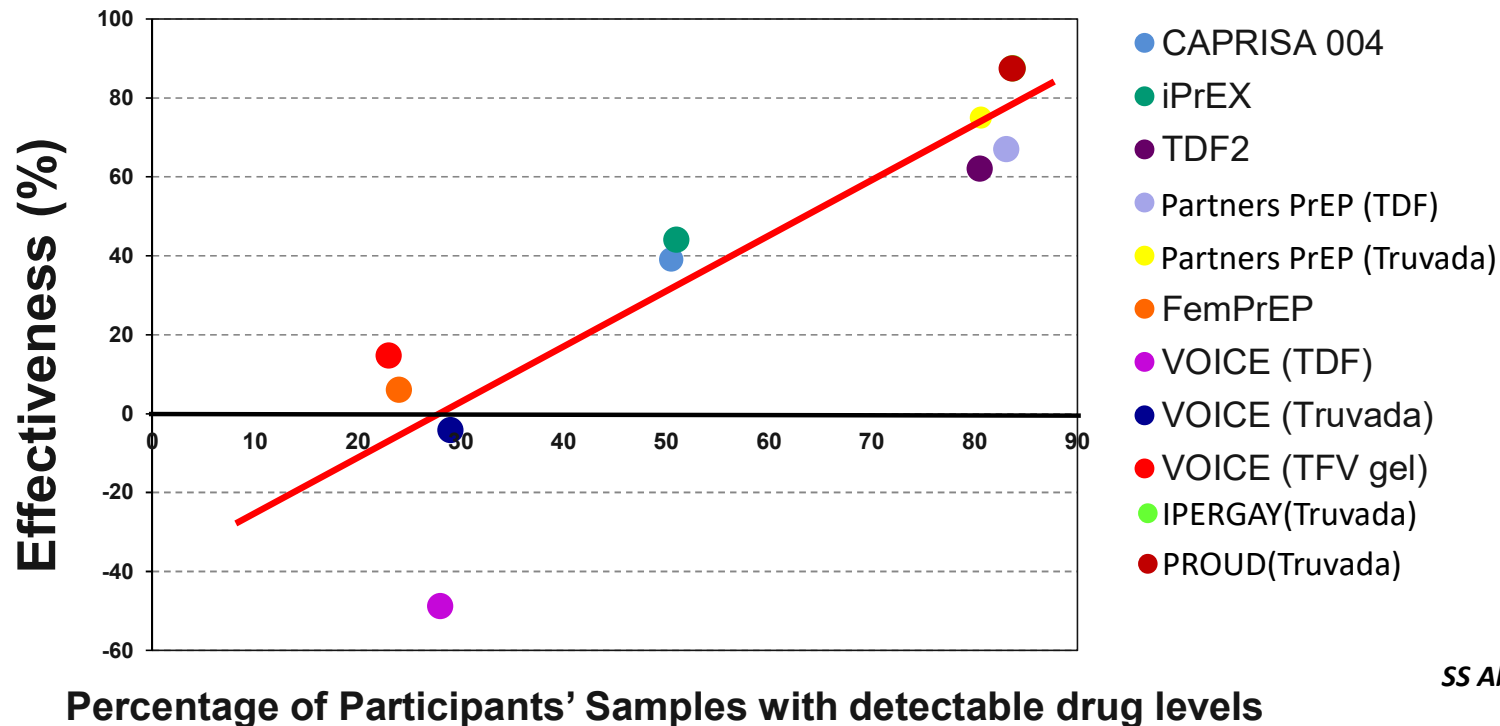


Garcia-Lerma, G and Heneine W
CDC, Division of HIV/AIDS Prevention, Laboratory Branch

Effectiveness of Daily TDF/FTC in Clinical Trials



Relationship Between Effectiveness and Adherence in Microbicide & PrEP Trials



SS Abdool Karim, personal
communication

Adherence and HIV Protection: Oral PrEP

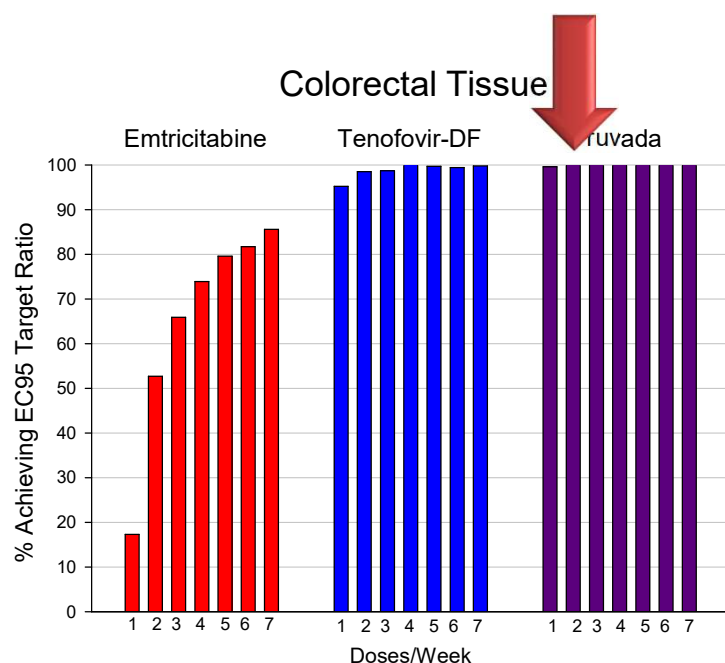
	% of blood samples with tenofovir detected	HIV protection efficacy in randomized comparison	HIV protection estimate with high adherence
Partners PrEP TDF/FTC arm	81%	75%	90% (tenofovir in blood)
TDF2	79%	62%	78% (prescription refill)
BTS (PWID)	67%	49%	70% - 84% (tenofovir in blood / pill count)
iPrEx	51%	44%	92% (tenofovir in blood)
FEM-PrEP & VOICE	<30%	No HIV protection	N/A

When adherence was high, HIV protection is consistent and high.

Baeten et al N Engl J Med 2012; Thigpen et al N Engl J Med 2012; Choopanya et al Lancet 2013;
Grant et al N Engl J Med 2010; Van Damme et al N Engl J Med 2012; Marrazzo et al CROI 2013

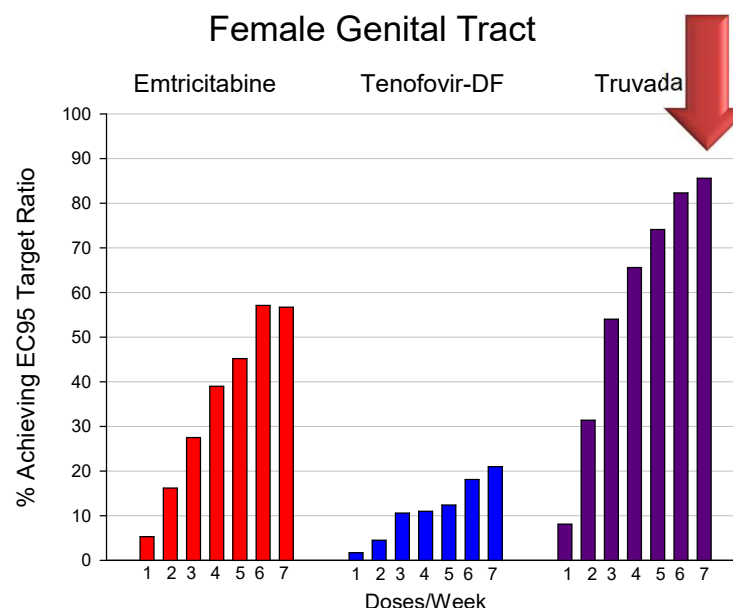
Achieving Steady State in Rectal vs FGT.

Cottrell et al J Infect Dis. 2016 Jul 1;214(1):55
Slide courtesy: Angela Kashuba



iPrEx OLE= ↓ HIV incidence by 90%
with 2 Truvada doses per week

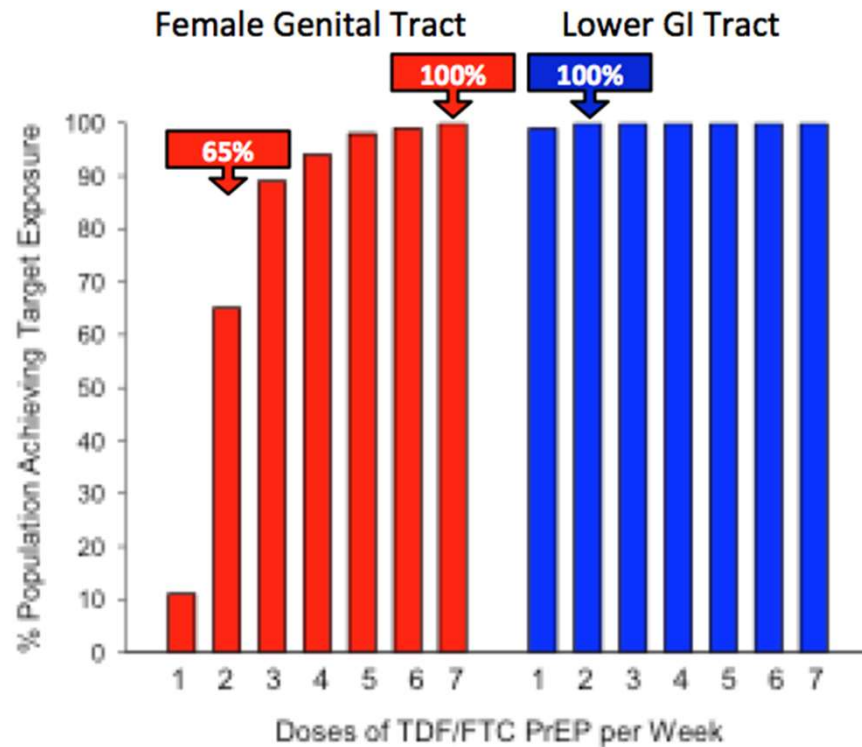
Anderson et al. Sci Transl Med Sep 12, 2012; 4(151): 151ra125.



Partners PrEP= ↓ HIV incidence by 90%
with 7 Truvada doses per week

Donnell D et. al. JAIDS. 2014;66(3):340-348.;

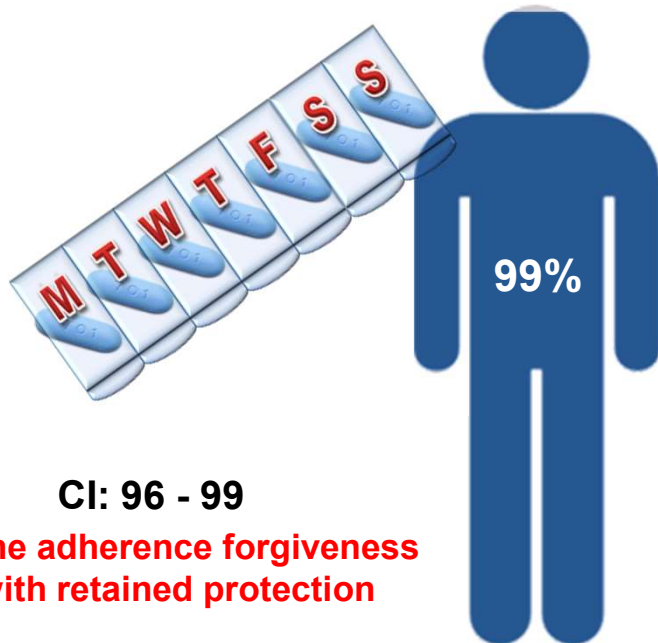
TDF/FTC PrEP for Women: Adherence



Cottrell ML et al. Predicting the Outcomes of HIV Pre-Exposure Prophylaxis Trials Using Tenofovir Disoproxil Fumarate \pm Emtricitabine in Men and Women. *Manuscript in development*. Preliminary results presented at: Cottrell et al. Predicting Effective Truvada® PrEP Dosing Strategies With a Novel PK-PD Model Incorporating Tissue Active Metabolites and Endogenous Nucleotides (EN). Abstract OA22.06 LB. HIV Research for Prevention (R4P) 2014, Cape Town, South Africa.

Maximizing the Potential Effectiveness

TDF/FTC (7x/week)

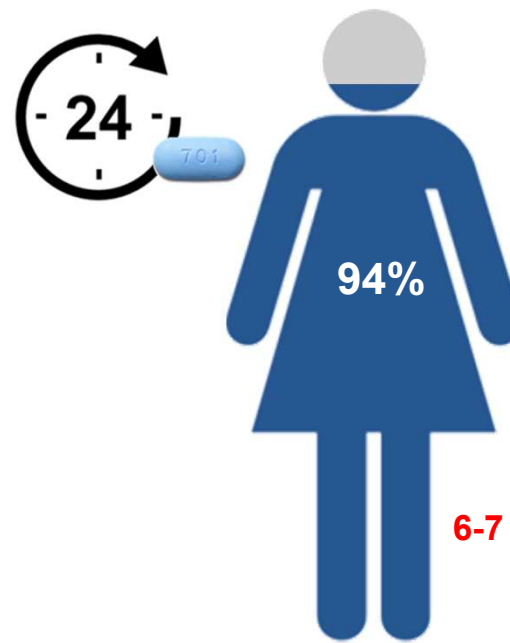


CI: 96 - 99

**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, JID, 2016.

Summary

- ✓ Prevention of HIV is an urgent priority- PREP is one tool
- ✓ Truvada is the only approved agent for HIV PREP
- ✓ Oral Truvada works as PrEP if taken daily
- ✓ Variability in Effectiveness in women may be due to factors like adherence, drug concentration in female genital tract

CDC recommendation:

When taken every day, Truvada as PrEP is safe and highly effective in preventing HIV infection.

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Thank you

Questions?

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