

# Case Three

**Can you prescribe PrEP for me ?**

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# Story

- A transgender woman (22 yrs old) has two regular sexual male partners (25 yrs. old and 50 yrs old). She has sexual relationship with the older man for 2-3 years and only for 6 months with the younger man. She feel that her younger lover seem to have a number of sexual partners with other gay men and women as well. Mostly he denied to use the condom when having sex with his partners include herself.

# Story

- She came to PIMAN (VCT) clinic in Chiang Mai to receive VCT last month. The HIV test result was negative but the counselor told her that since she often had sexual intercourse (mostly was receptive anal sex) with her younger partner without using condoms most of the times in the last six months, so she may or may not have the HIV positive result since it can be during the window period.

# Story

- The counselor encouraged her to use condoms all the times when she will have sex with her partner and ask her to come back for the HIV test again in the next 3 months. (For her older sexual partner, he always asked to use the condom when having sex with her.)

# Story

- Since she knew about the result of iPrEX study at PIMAN clinic but she didn't involve as the participant in the past, so she asked the doctor to prescribe Truvada for her.
- She feel afraid that she may get HIV infection from her male partners someday in the future.

# Should doctor prescribe PrEP for her ? ( The BEST one !)

- **A.** No. Suggest her to separate from her younger lover. Go with the older one only.
- **B.** Emphasize her to use condom all the times.
- **C.** Prescribe Truvada for one month and ask her to come back for HIV test.
- **D.** Need to make sure that she was not in the window period before start PrEP.
- **E.** Provide Male circumcision for her partners.

# People who have a chance to be infected with HIV in their life?



It doesn't matter what genders you are, but how **you and your partner** behave together when having **SEX** to protect yourself from **GETTING HIV** infection

**When people said  
:-They always use  
the condom when  
have SEX ?**

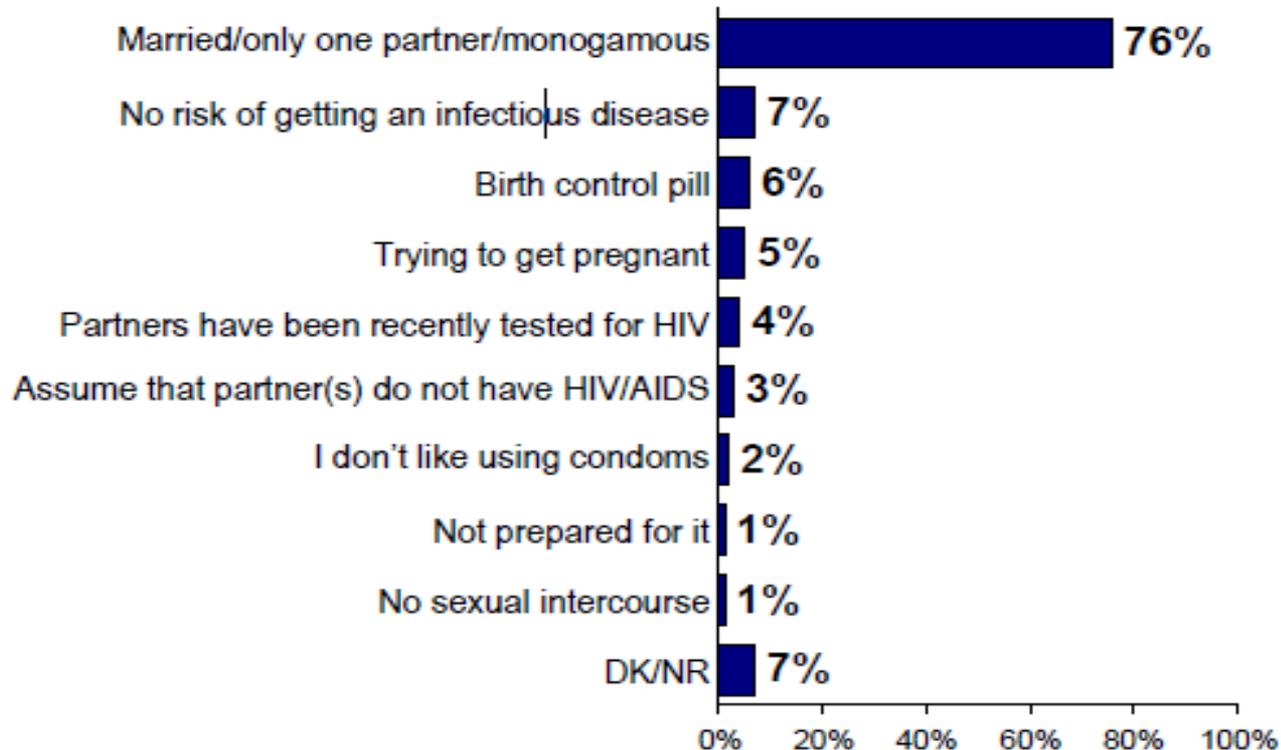
**What does it really  
mean to you ?**



# Can't we just promote condoms?

## Motivation Regarding Safer Sex

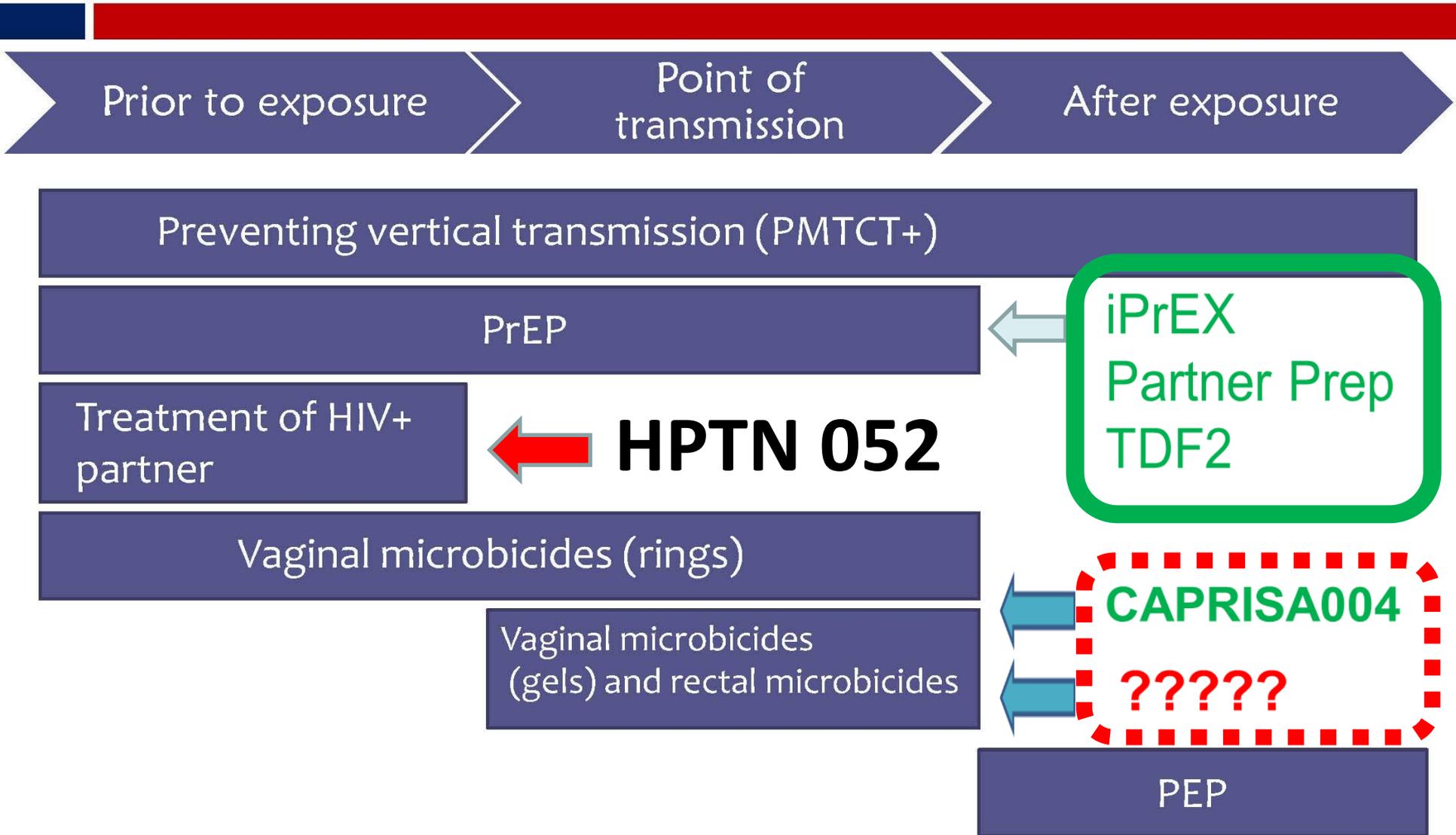
“Why didn't you use a condom?”



# PRE-EXPOSURE PROPHYLAXIS (PrEP)

- 🚫 PrEP use for people who are vulnerable to get DISEASE
- 🚫 PrEP is the long term exposure to a prophylactic treatment (*drugs*) of a disease prior to exposure to the cause of that disease. (eg; virus, bacteria, protozoa, etc)
- 🚫 The prophylactic treatment (*drugs*) will already be in place when exposure occurs, and may either be able to prevent infection or treat it.
- 🚫 PrEP (ARV drugs) is a potential new HIV prevention intervention that could have an important impact on HIV prevention globally in the FUTURE !!.

# ARV-based prevention options



# Strategies for PrEP trials

- **Oral PrEP :-**
  - ARVs taken regularly  
(daily, intermittent ?)
- **Topical PrEP :-**
  - ARV-based microbicides**
    - ARVs gels in vagina
    - ARV vaginal rings or
    - other products  
(Vagina/Rectum)



# TDF and FTC/TDF for PrEP

Among the anti-HIV medications currently available, two most used in animal and human trials of PrEP:



= TDF (tenofovir), in 1% gel or as oral tablet



= FTC/TDF (co-formulated emtricitabine + tenofovir)

\* TDF: tenofovir disoproxil fumarate: *Viread*®

\* FTC: emtricitabine: *Emtriva*®

\* TDF/FTC: *Truvada*®

# 2010 was a very good year!

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*Two studies provided proof of concept for ARV-based prevention*

## □ CAPRISA 004

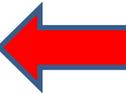
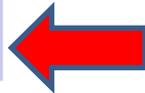
- Tenofovir gel resulted in **39% HIV reduction** among high-risk women who used it before and after sex

## □ iPrEx

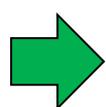
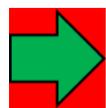
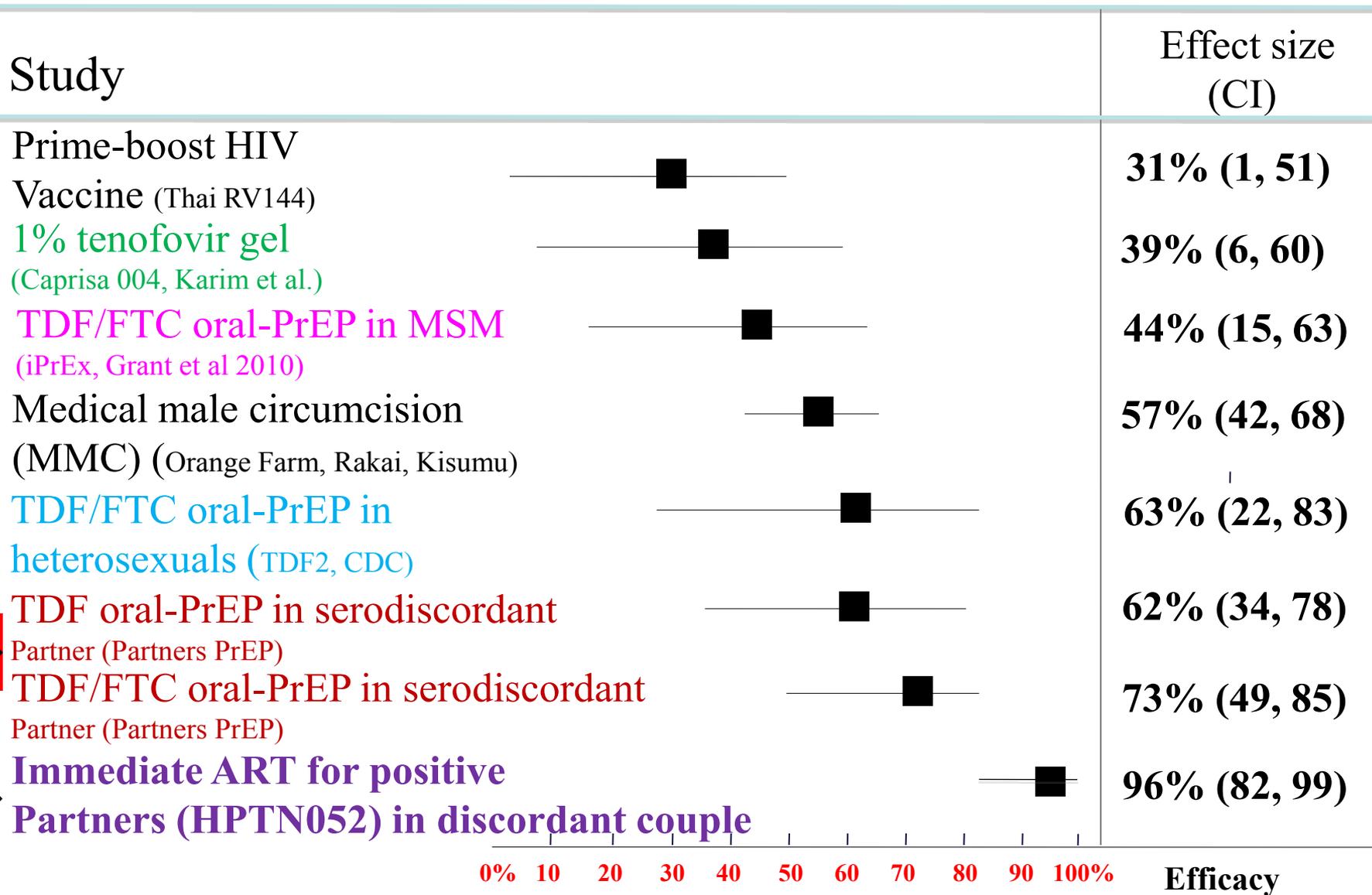
- Truvada used daily among men who have sex with men resulted in **44% reduction** in HIV



# 2011; exciting year for PrEP

- **FEM-PrEP study stopped for futility**
  - April 18<sup>th</sup>, 2011
- **HPTN-052 delayed treatment arm stopped for efficacy (Rx as Prevention)** \* HIV Discordant couples 
  - May 12<sup>th</sup>, 2011
- **Partners PrEP placebo arm stopped for efficacy** \* HIV Discordant couples 
  - July 13<sup>th</sup>, 2011
- **CDC announce positive TDF2 results**
  - July 13<sup>th</sup>, 2011
- **VOICE study stop the tenofovir arm, Gel**
  - Sep 28<sup>th</sup> 2011, and then Nov 2011

# New biomedical intervention strategies



# PrEP adherence critical for efficacy

Trial	Population	Overall efficacy (miTT)	Estimated risk reduction with drug detection
iPrEx	2,499 MSM	42%	<b>92% risk reduction</b> with detectable drug
Partners PrEP	4758 heterosexual discordant couples	TDF: 67% FTC/TDF: 75%	<b>90% risk reduction</b> with detectable drug
TDF2	1200 heterosexual men and women	62%	<b>78% risk reduction</b> excluding participants with no refills for >30 days
Fem-PrEP	2120 high-risk women	<b>Study stopped due to futility</b>	<b>&lt;26% women</b> in FTC/TDF group had consistently detectable drug; “adherence too low to assess efficacy”

# Analysis Confirms Link Between PrEP Adherence and Reduced HIV Risk, Estimates Effective Dosing

Details Category: [HIV Prevention](#) Published on Thursday, 20 September 2012 00:00 Written by pr



In the new substudy analysis, published in the [September 12, 2012, issue of \*Science Translational Medicine\*](#), researchers found that men would have to take Truvada at least 4 days per week to achieve 90% or better risk reduction, while taking the drug every day was associated that nearly complete protection.

other day.

Science  
Translational  
Medicine



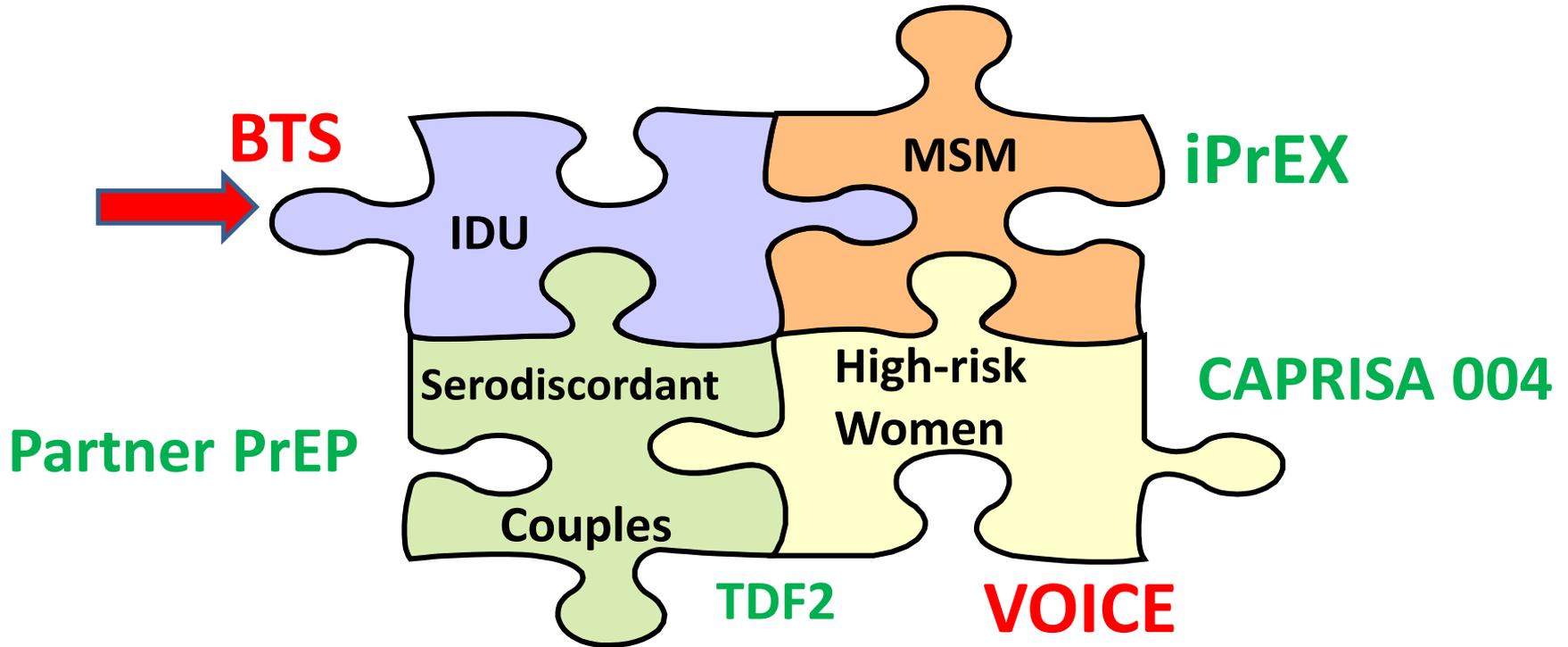
**Emtricitabine-Tenofovir Concentrations and Pre-Exposure Prophylaxis Efficacy in Men Who Have Sex with Men**

Peter L. Anderson *et al.*

*Sci Transl Med* **4**, 151ra125 (2012);

DOI: 10.1126/scitranslmed.3004006

# Ongoing PrEP trials will complete different parts of the 'PrEP Puzzle'



**Safety, adherence, & efficacy**

# FDA Advisory Committee: May 10, 2012

## Truvada® tablets be approved for PrEP in:

- Men having sex with men
- HIV (-) negative partners in serodiscordant couples
- Others at risk due to sexual activity

**Tenofovir vaginal gel or oral tablets are not candidates for approval as PrEP at this time**



U.S. Food and Drug Administration

## *FDA is requiring Truvada's manufacturer to collect certain post-marketing data to help evaluate the drug's use for a PrEP indication in real-world practice.*

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of becoming infected with HIV and the development of drug-resistant variants if they continue taking Truvada after becoming infected with HIV.

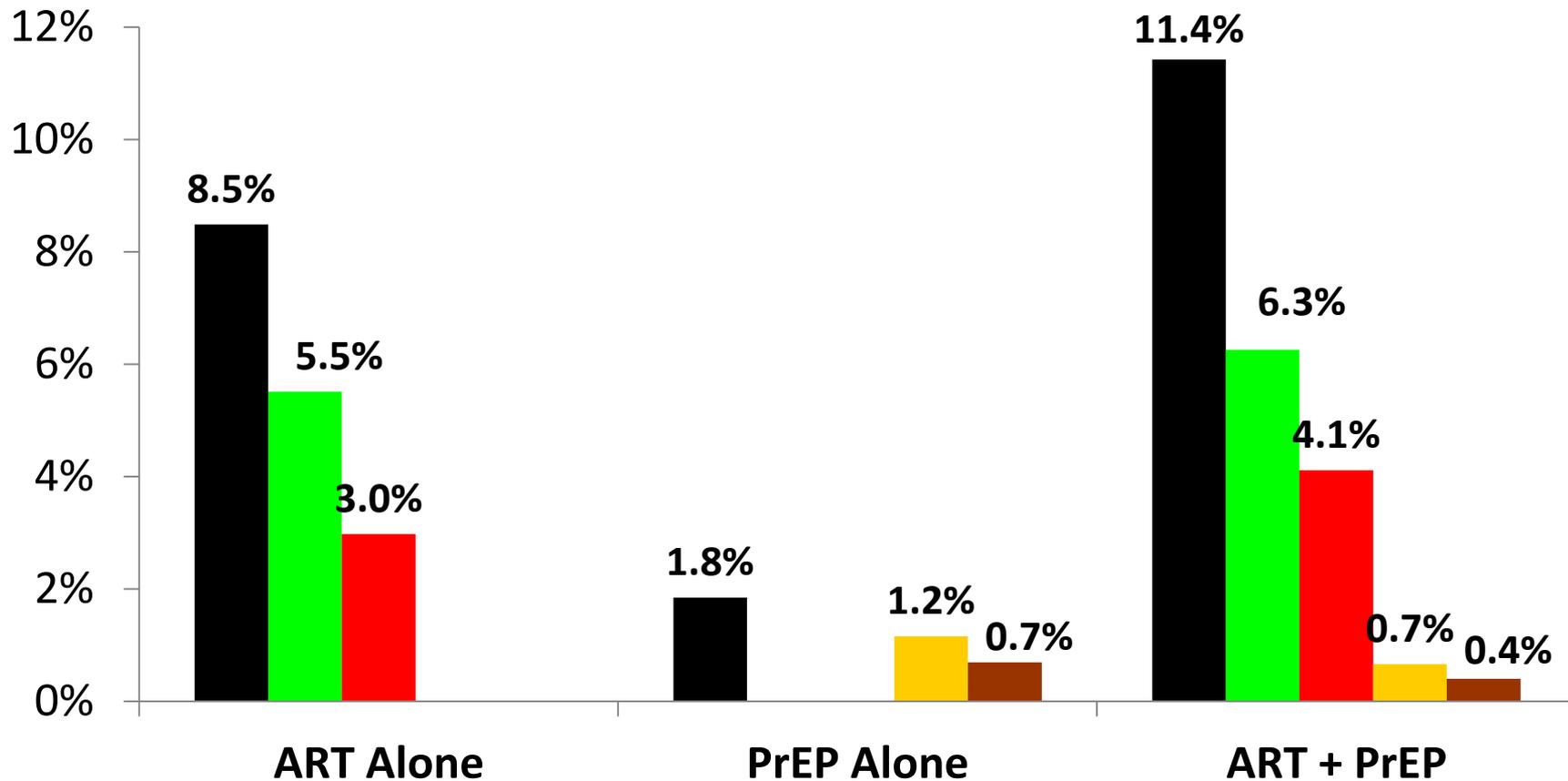
- Prescriber training and education targets likely prescribers of Truvada for PrEP. This program includes:

care professionals, and uninfected individuals about the risks of Truvada for a PrEP indication. If the FDA determines the REMS is not meeting its goals, the agency will re-evaluate the program and take appropriate action to ensure safe use of the drug.

# 5 key challenges in PrEP & TasP:

1. **Adherence:** Will healthy people be willing to take medication everyday for decades?
2. **Safety:** Are ARVs safe in long-term?
3. **Resistance:** Will HIV infection on PrEP cause ARV resistance & will TasP lead to widespread resistance with poor adherence in well people?
4. **Displacing condoms:** Will there be behavioural disinhibition / risk compensation?
5. **Cost and Health service burden:** Can we afford large populations on ARVs as PrEP or TasP?

# Prevalent Cases of Drug Resistance, 2022



■ Overall Drug Resistance

■ ART Acquired Resistance

■ ART Transmitted Resistance

■ PrEP Acquired Resistance

■ PrEP Transmitted Resistance

# Goals of topical & oral ARVs for HIV prevention

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- **Right drug**

(safe, effective, minimal resistance)

- **Right place**

(sufficient concentrations at site of exposure)

- **Right time**

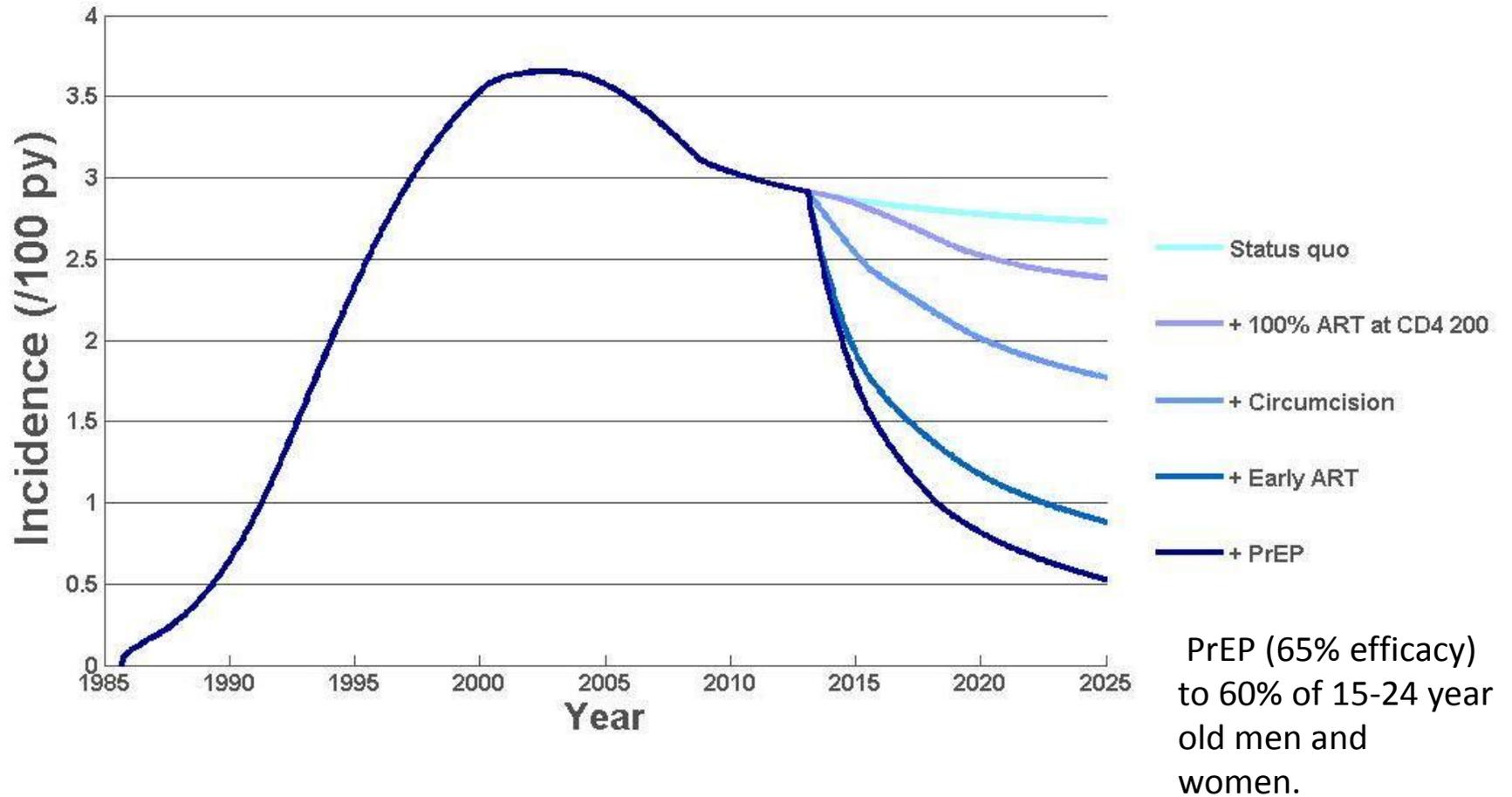
(short onset of activity & long half-life  
to optimize efficacy with variable adherence)

# Key Implementation Questions for TDF gel & oral FTC/TDF

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- **Whom to target?**
  - Who is high risk? How to ascertain?
  - HIV discordant couples?
  - Heterosexual populations – no data currently
- **Where to deliver?**
  - STD clinics? HIV clinics?
  - Public health facilities? Primary care clinics? Pharmacies?
- **For public health (i.e., not “boutique”) impact = high access and coverage of highest risk persons is required**

# Math Model of Impact of Combination Prevention



Hallett, T., et al., Imperial College London (2011)

# Should doctor prescribe PrEP for her ? ( The BEST one !)

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- **B.** Emphasize her to use condom all the times.
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- **D.** Need to make sure that she was not in the window period before start PrEP.
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# Should doctor prescribe PrEP for her ? ( The BEST one !)

- **A.** No. Suggest her to separate from her younger lover. Go with the older one only.
- **Answer : - Easy to say, difficult to do**
- **B.** Emphasize her to use condom all the times.
- **Answer :- How to make it possible.**

# Should doctor prescribe PrEP for her ? ( The BEST one !)

- **C.** Prescribe Truvada for one month and ask her to come back for HIV test.
- **Answer :- Need to aware acute HIV infection**
- **D.** Need to make sure that she was not in the window period before start using PrEP.
- **Answer :- RIGHT APPROACH but HOW?**
- **E.** Provide Male circumcision for her partners.
- **Answer E:- No help to prevent transmission**

# During PrEP

- **HIV test every 3 months (or less if ANY INDICATION for acute HIV infection !)**
- **Drug Adherence counseling every visit (Need to emphasize to take a pill / day)**
- **Risk reduction counseling every 3 mns.**
- **Creatinine/BUN at 3 months and yearly**

# **Discontinue PrEP**

- **Test for HIV (Should provide VCT services q 6 months).**
- **Risk reduction counseling at stop visit and discuss other HIV prevention tools.**
- **Link into care if HIV positive and check for drug resistance (if possible).**

# Summary: ARVs for prevention in 2013

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- Roll-out of PrEP will be complex: **Demonstration projects to inform effective implementation**
- Future is exciting with difficult challenges: **Prioritization & efficient testing of new products, delivery modes, & integration into combination prevention**
- Treatment is prevention: **HPTN 052 confirms observational data; need to expand ART coverage**

# For more information...

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- PrEP: [www.prepwatch.org](http://www.prepwatch.org)
- Microbicides
  - [www.global-campaign.org](http://www.global-campaign.org)
  - [www.rectalmicrobicides.org](http://www.rectalmicrobicides.org)
  - [www.ipm-microbicides.org](http://www.ipm-microbicides.org)
  - [www.microbicide.org](http://www.microbicide.org) (Alliance for Microbicide Development)
- Treatment of HIV+ partner
  - [www.hptn.org](http://www.hptn.org) (look under HPTN052)