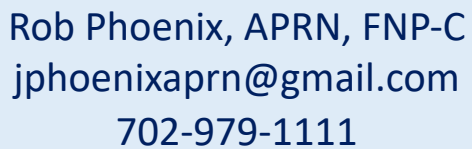




HIV Treatment & HIV prevention in 2018

Rob Phoenix, APRN, FNP-C
Huntridge Family Clinic





702-979-1111

Disclosure

1

Speaker Bureau:
Gilead Science
Napo Pharmaceutical

2

Consultant:
Gilead Science
Napo Pharmaceutical

3

Principle Investigator
on Gilead Science
sponsored HIV
prevention and
treatment studies

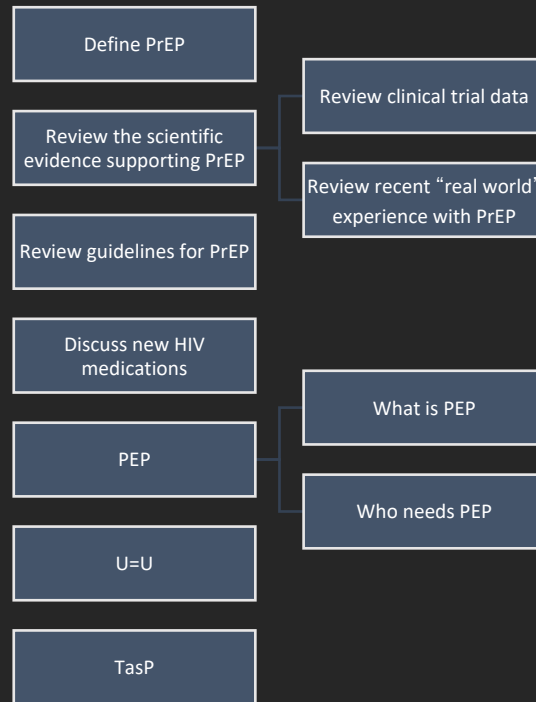
4

Principle Investigator
for Investigator
sponsored research on
nPEP/PrEP

5

Off label medication
discussion for PEP

Objectives



Breaking down the word

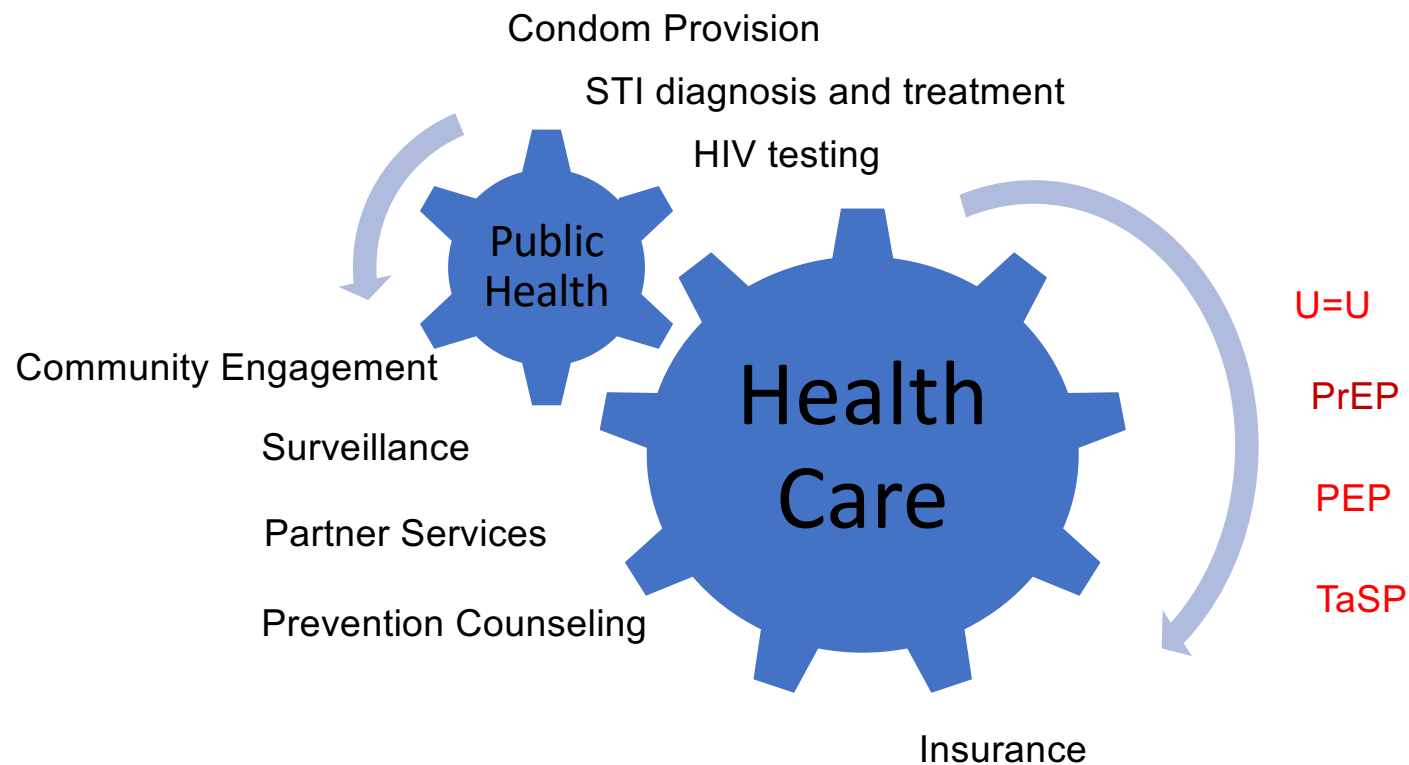
Pre — meaning BEFORE

Exposure — activity that can lead to HIV infection

Prophylaxis — meaning protection

Protect yourself BEFORE you are exposed

Integrating and Leveraging Biomedical HIV Prevention



UNDETECTABLE = UNTRANSMITTABLE



Bruce Richman
September 2017

The Pivotal HPTN 052 Study



The
New England
Journal of Medicine

Vol. 365

August 11, 2011

Number 6

Prevention of HIV-1 Infection with Early Antiretroviral Therapy

HPTN 052 Study Team

- 1,763 HIV-serodiscordant couples in 9 countries
- 96% reduction in HIV transmission when ART started in HIV-infected partner at CD4 count



The
New England
Journal of Medicine

Vol. 375

September 1, 2016

No. 9

Antiretroviral Therapy for the Prevention of HIV-1 Transmission

HPTN 052 Study Team

- During the 4-year follow-up period, the protective effect was sustained
- Overall, early ART reduced HIV transmission to uninfected

PARTNER Study



Sexual Activity Without Condoms and Risk of HIV Transmission in Serodifferent Couples When the HIV-Positive Partner Is Using Suppressive Antiretroviral Therapy

AJ Rodger, J Lundgren et al.

- After ~58,000 condomless sex acts, no linked HIV transmissions with HIV+ partner on suppressive ART

Opposites Attract Study – No HIV Transmissions When HIV+ Partner Had Undetectable Viral Load



IAS2017

IAS 2017, Paris

July 25, 2017

B Bavinton et al.

Abstract # TUAC0506LB

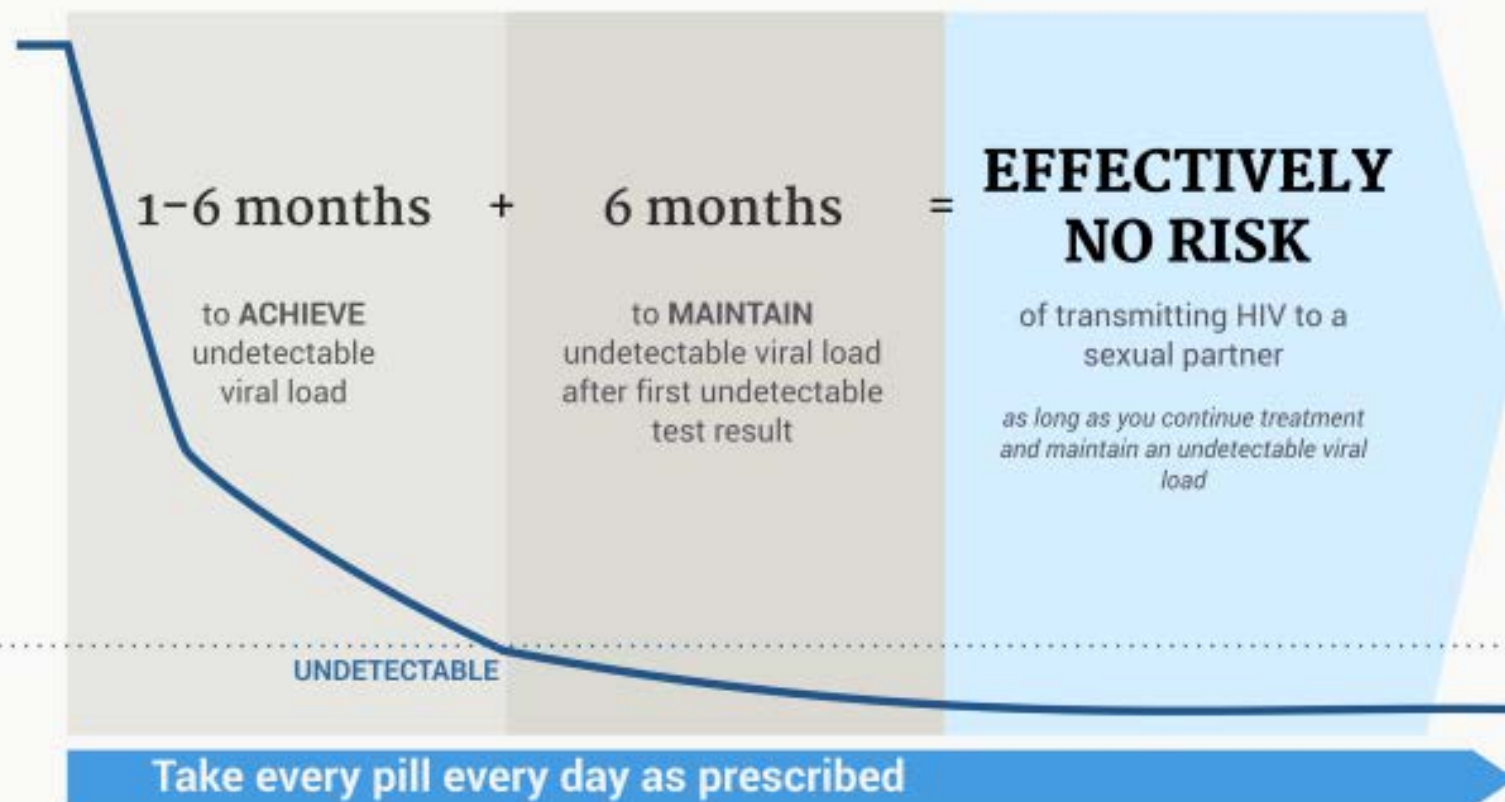
- 358 HIV-serodiscordant MSM couples in Australia, Thailand and Brazil
- 16,889 acts of condomless anal intercourse
- No linked HIV transmissions in 591 couple-years of followup

- Partner 1
 - 9/10 to 5/14
 - 888 couples
 - 337 gay

estimated total of 76,991
condomless sex acts, produced
no transmission between
partners.

- Partner 2
 - 5/14 to 4/18
 - 635 gay

Partners Study



What Is PrEP?

Pre-exposure
Prophylaxis: A
pharmacologic HIV
prevention
intervention for
persons at high risk of
becoming infected with
HIV.



An HIV-uninfected
individual takes
antiretroviral
medication(s) *before*
potential HIV exposure



The use of medication
for prophylaxis is well
established:

- Use of contraceptive methods to prevent pregnancy
- Use of antimalaria medications before traveling to endemic areas

What is PrEP?

- Pre Exposure Prophylaxis
- Truvada (tenofovir, emtricitabine)
- Once daily pill that **prevents** HIV
 - CDC: reduces the risk of HIV infection by up to 92%
 - Effectiveness differs based on anatomy
- PEP
 - Post Exposure Prophylaxis



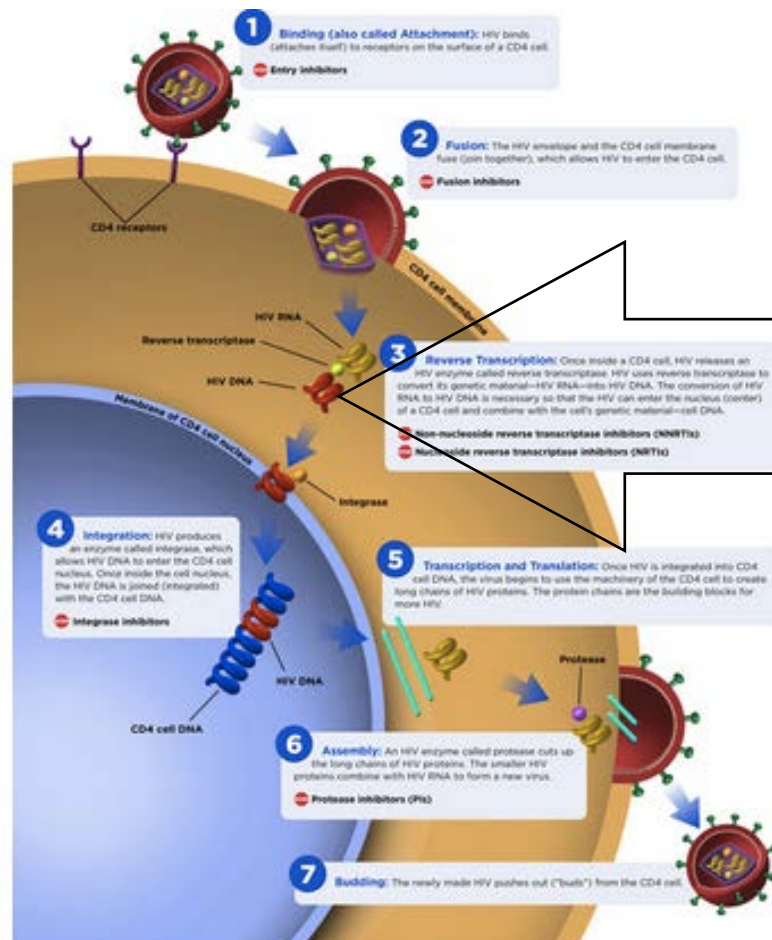
Why TRUVADA (TVD) for Pre-exposure Prophylaxis (PrEP)?



TRUVADA is indicated in combination with safer sex practices for PrEP to reduce the risk of sexually acquired HIV-1 in adults at high risk

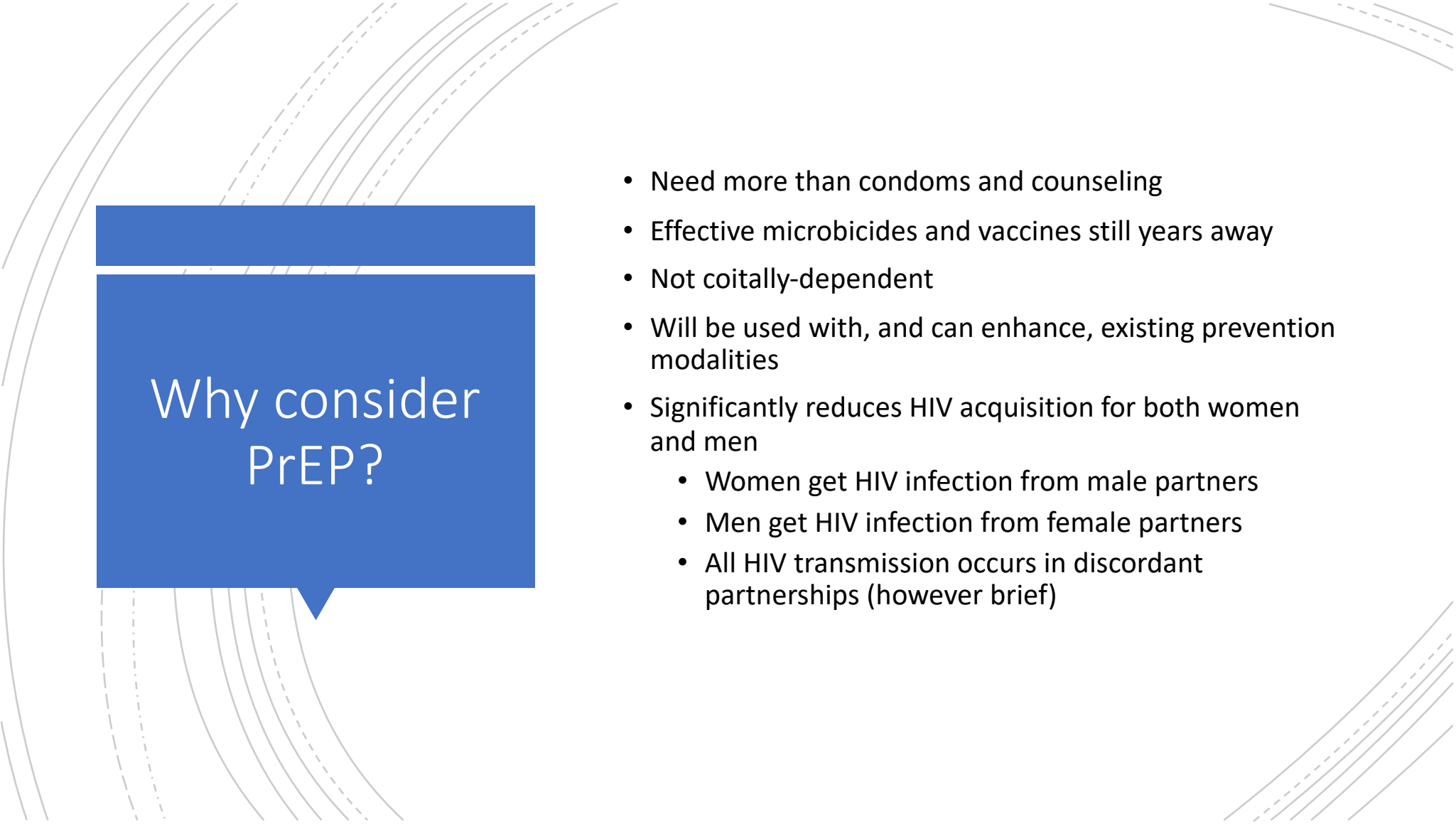
1. Garcia-Lerma J, et al. *Trends Pharmacol Sci* 2009; 31(2): 74-81
2. Chirenje Z, et al. *Expert Rev. Anti Infect Therap* 2010; 8(10): 1177-86.
3. Data on File Feb. 2015.
4. TRUVADA Prescribing Information. Gilead Sciences, Inc. 2013.
5. Cohen MS, et al. *Ann Intern Med.* 2007;146:591-601.

Efficacy	<p>Pre-Clinical</p> <ul style="list-style-type: none"> • Tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) have long intracellular half-lives (40 to >100 hours)¹ • TDF and FTC effectively prevented infection in non-human primate studies²
Safety	<ul style="list-style-type: none"> • TVD has favorable safety and tolerability profile²⁻⁵ • TDF and FTC: approved in 2001 and 2003, respectively, for treatment of HIV³ and 2012 for PrEP <ul style="list-style-type: none"> ▪ TDF: ~9 million patient-years; FTC: ~6 million patient-years (in the commercial or clinical study settings)³ ▪ TDF: High barrier to resistance and limited cross-resistance⁵
PK	<ul style="list-style-type: none"> • TVD is one pill, once daily⁴ • TVD can be given with or without food⁴ • TFV and FTC concentrations in the genital tract exceed those in blood plasma⁵



NRTI's and NNRTI's work here

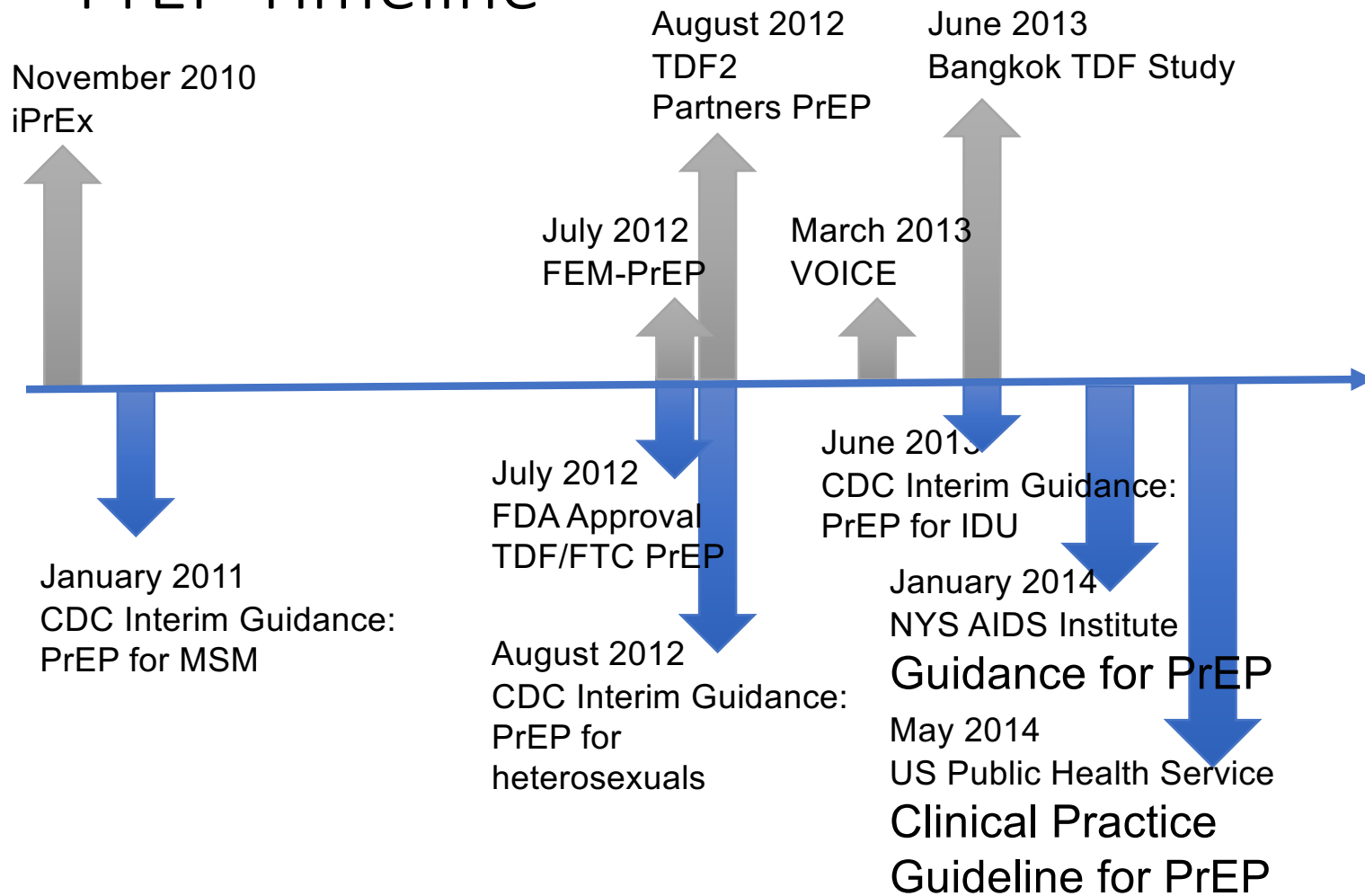
<http://www.aidsinfo.nih.gov/education-materials/fact-sheets/19/73/the-hiv-life-cycle>



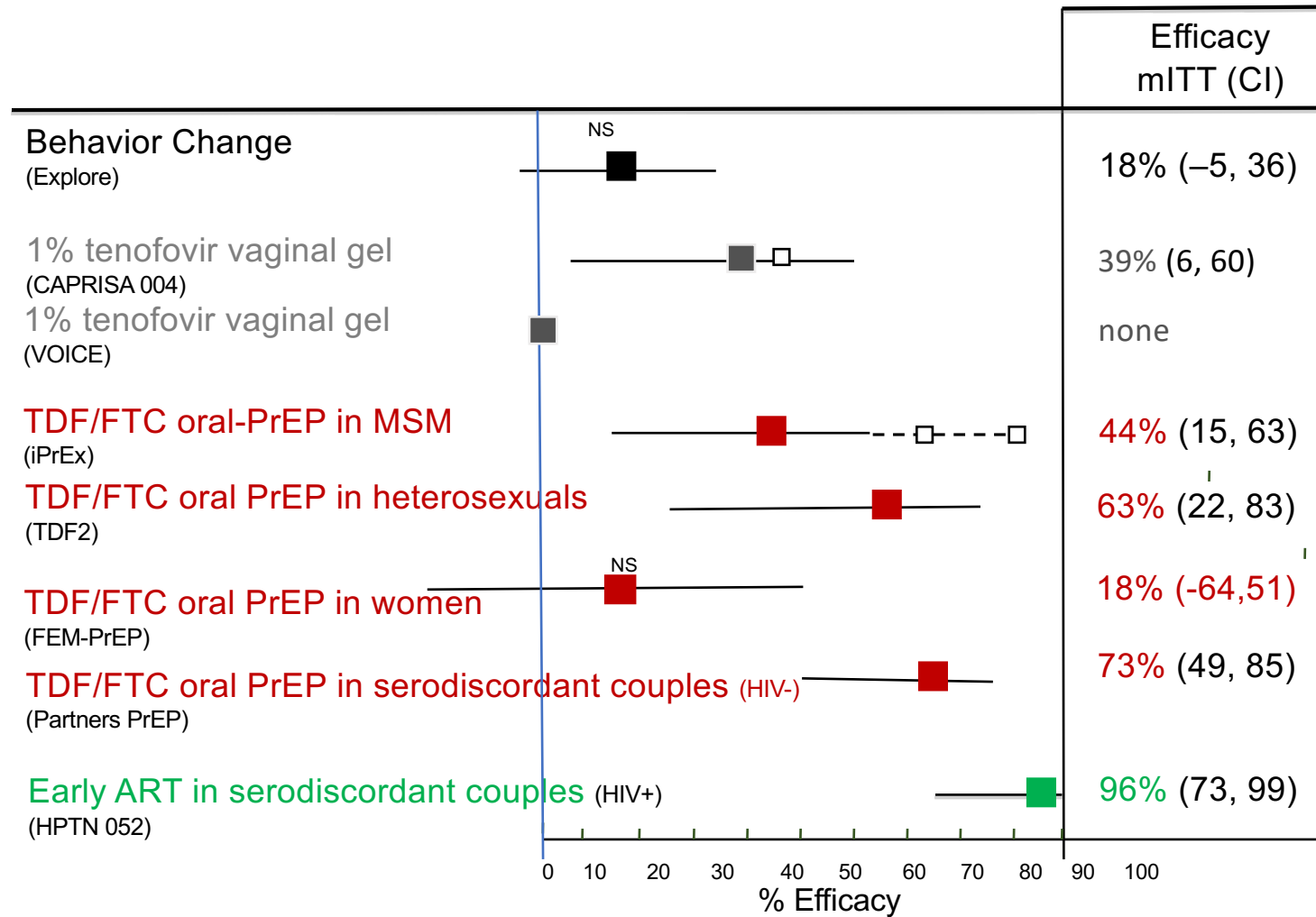
Why consider PrEP?

- Need more than condoms and counseling
- Effective microbicides and vaccines still years away
- Not coitally-dependent
- Will be used with, and can enhance, existing prevention modalities
- Significantly reduces HIV acquisition for both women and men
 - Women get HIV infection from male partners
 - Men get HIV infection from female partners
 - All HIV transmission occurs in discordant partnerships (however brief)

PrEP Timeline



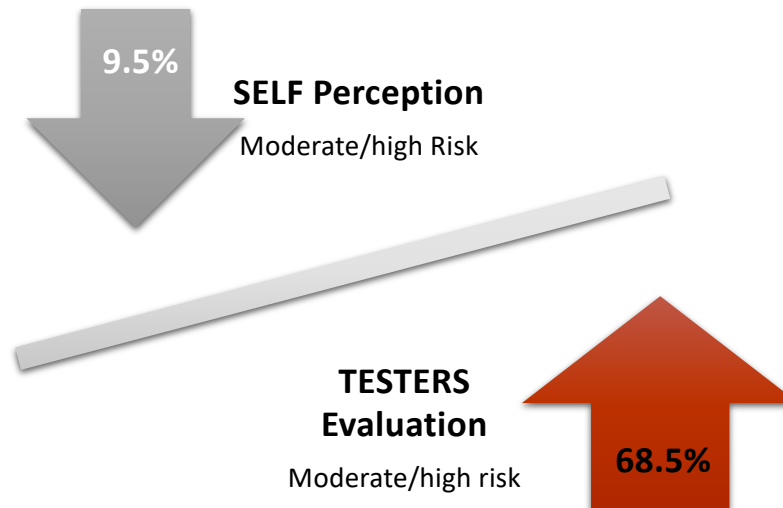
Key Prevention Trials



Self Perception of HIV

Risk is Low

Persons (N=3,533; >90% African-American) undergoing HIV rapid testing in Philadelphia were surveyed between July 2012 and Dec 2013

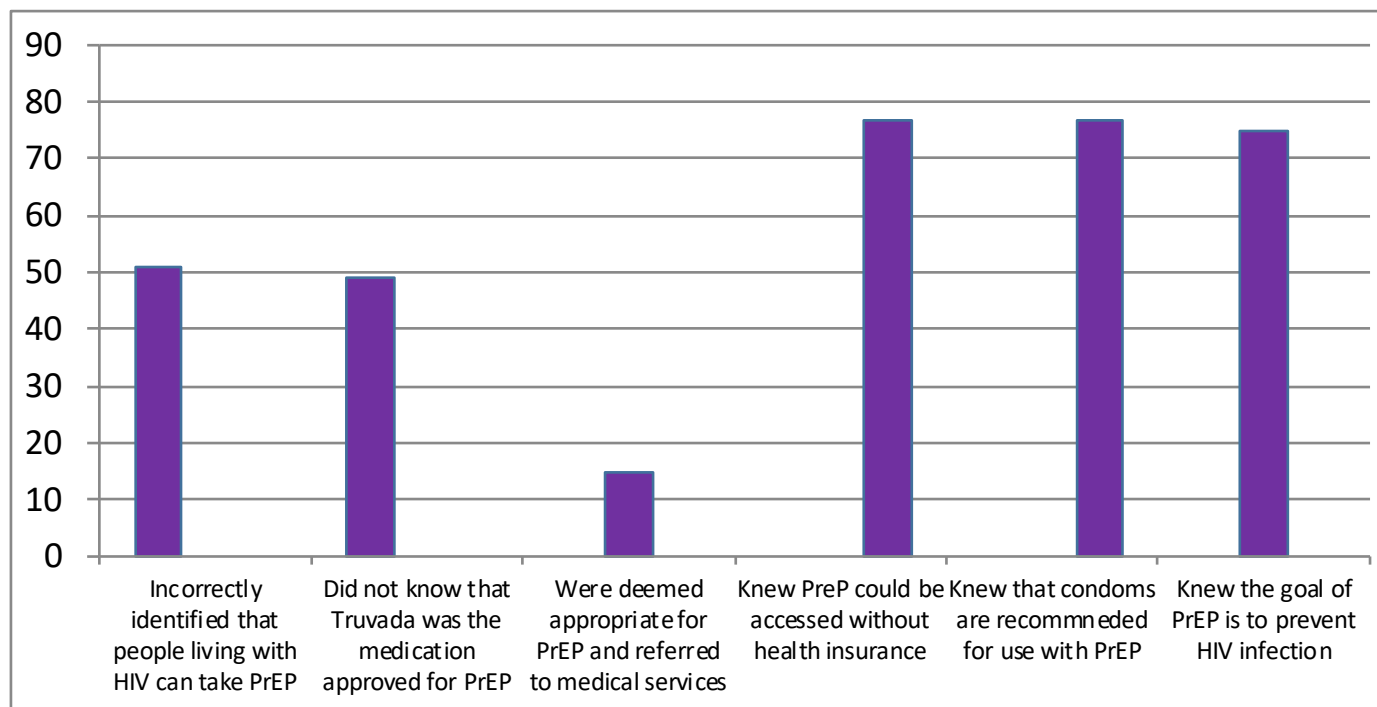


A large proportion of patients at high-risk for HIV infection do not perceive themselves at high risk

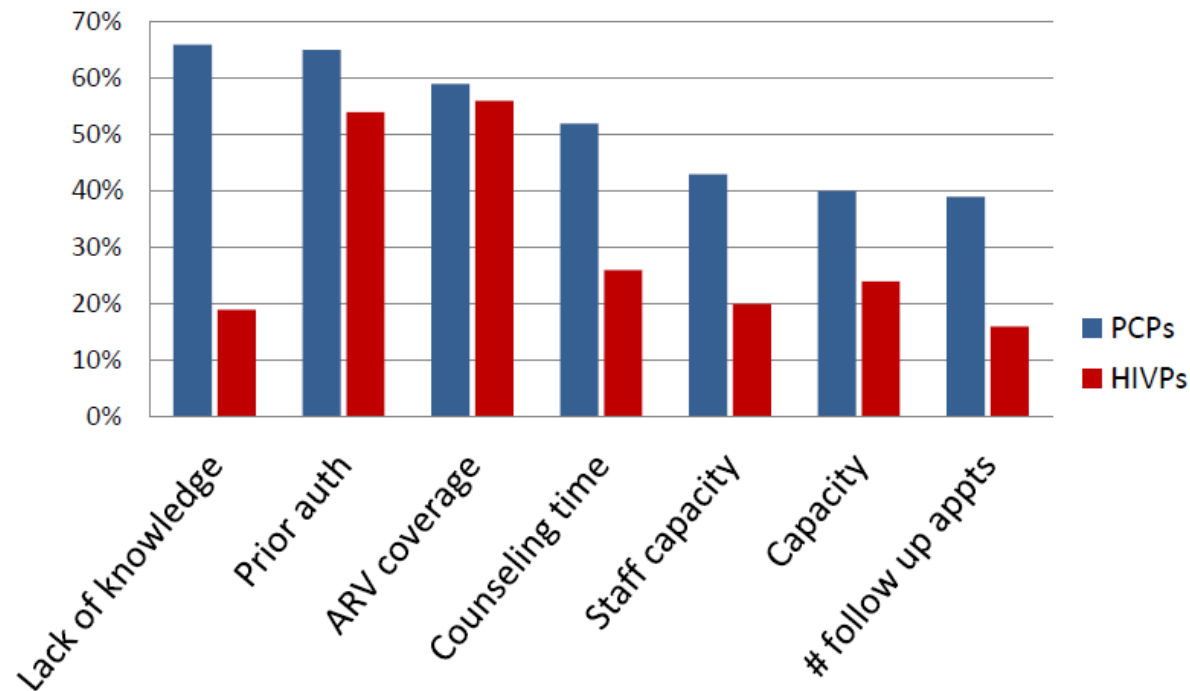
KwaKwa et al. IAC 2014 Melbourne, Australia

Community Understanding of PrEP is Low

PrEP awareness survey of MSM seeking HIV testing in
NYC from Feb-Aug, 2015



Provider reported barriers to PrEP implementation



Primary care providers identify more barriers to implementing PrEP than HIV Providers

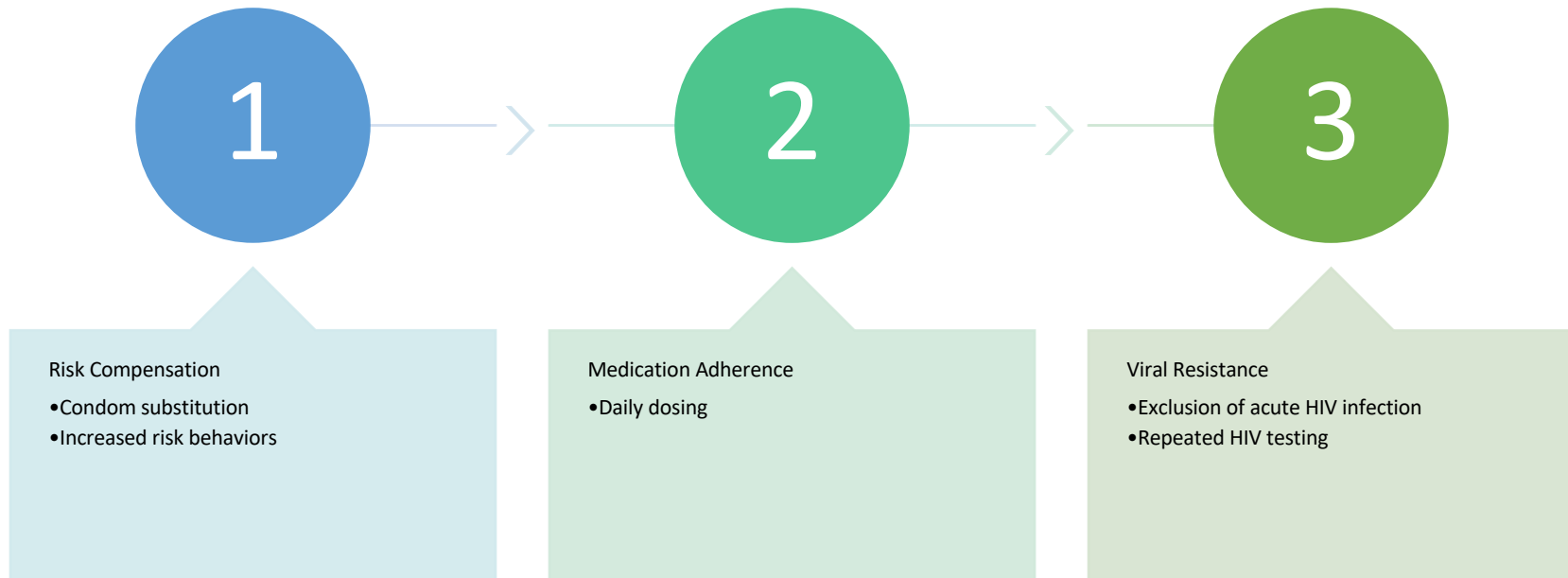
HIV Providers (HIVP) n = 245
Primary care providers (PCP) n = 280

Petroll, A et al; GLMA2015

PrEP: Benefits and risks

- Primary care benefits
 - hepatitis vaccination, reproductive health care
- Cost-effective
 - Yes, if targeted to those with high incidence
- Resistance
 - Uncommon if screening for acute infection
- Toxicities/side effects
 - Few, mild, and transient
- Adherence
 - Poor in some trials, high in others
- Risk compensation
 - Not seen (yet), models suggest unlikely to exceed benefit

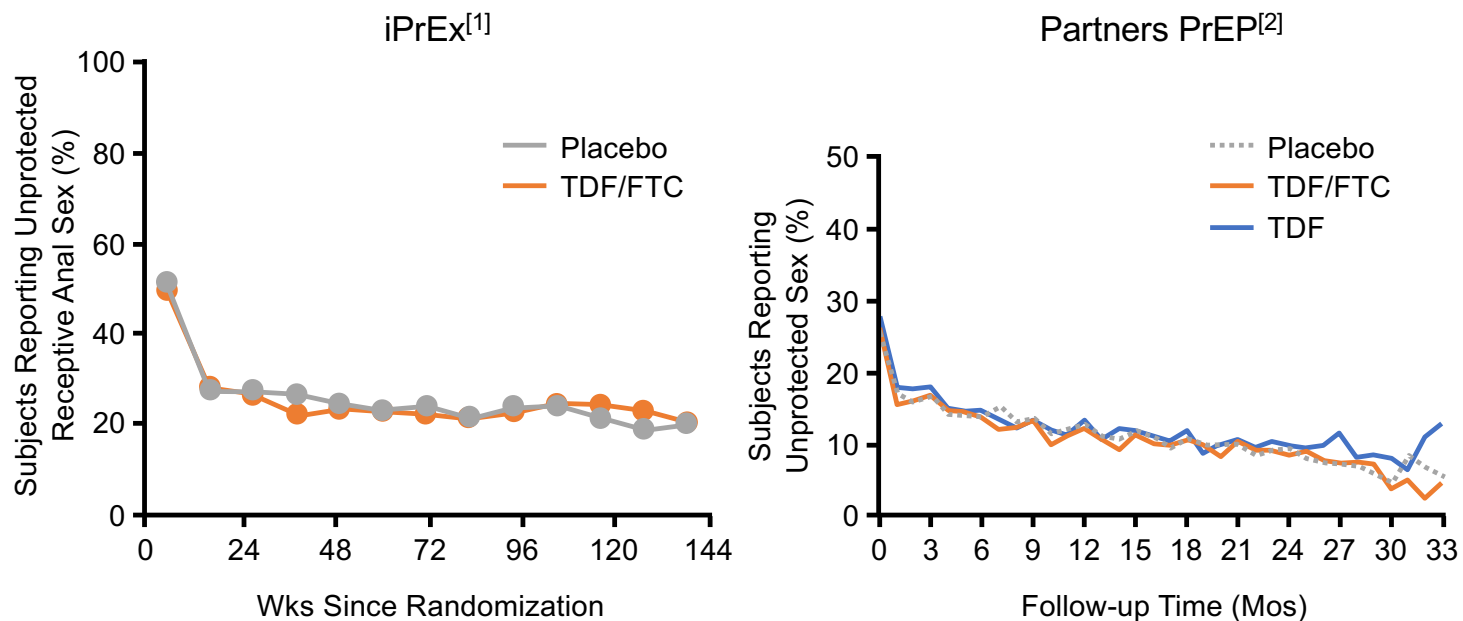
Key Concerns for the Safe and Effective Use of PrEP





Risk Behavior

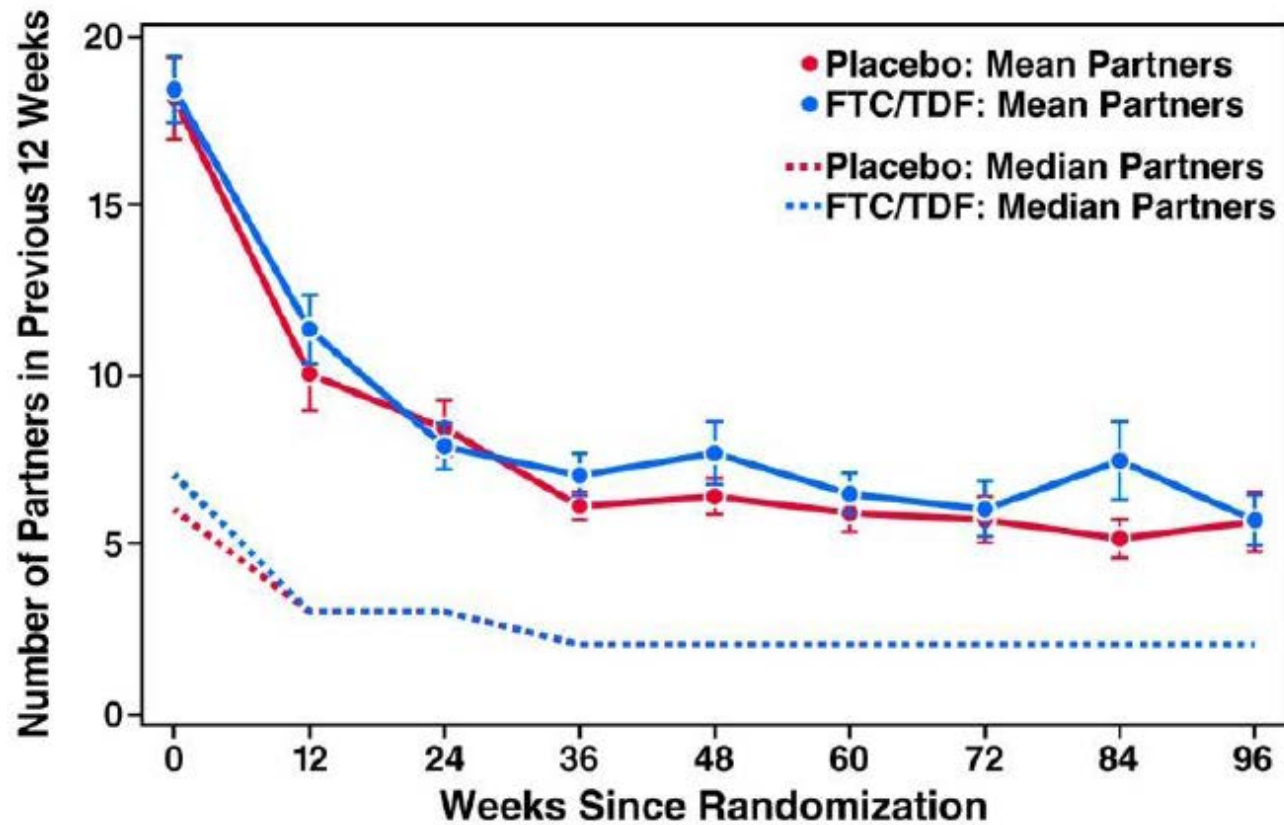
PrEP Trials Found *Decreasing* Risk Behavior Over Time



1. Grant RM, et al. N Engl J Med. 2010;363: 2587-2599.

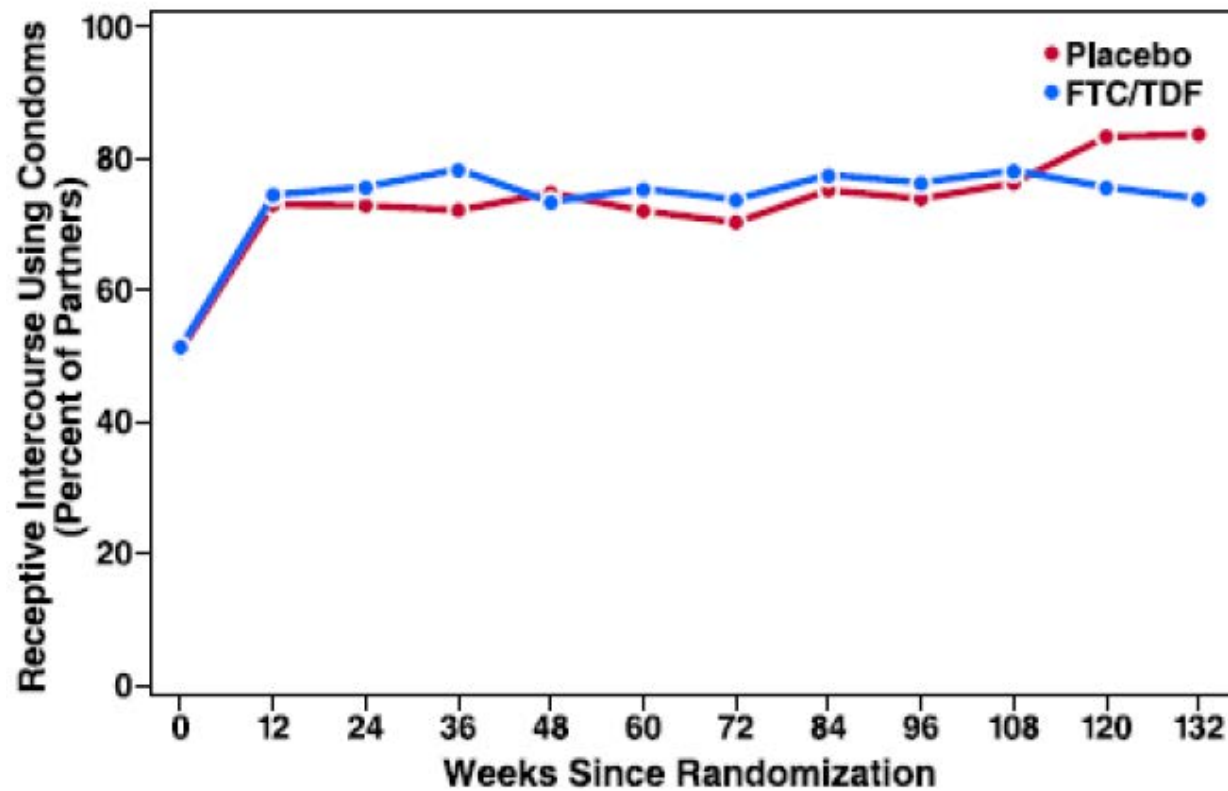
2. Baeten JM, et al. N Engl J Med. 2012;367:399-410.

Risk Behavior: Partners decreased



NEJM, Nov 23, 2010

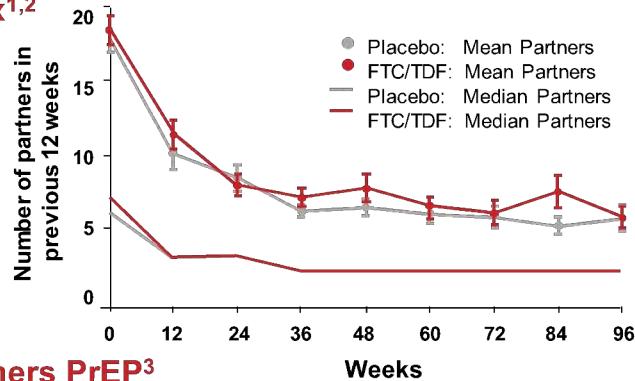
Risk Behavior: Condom use increased



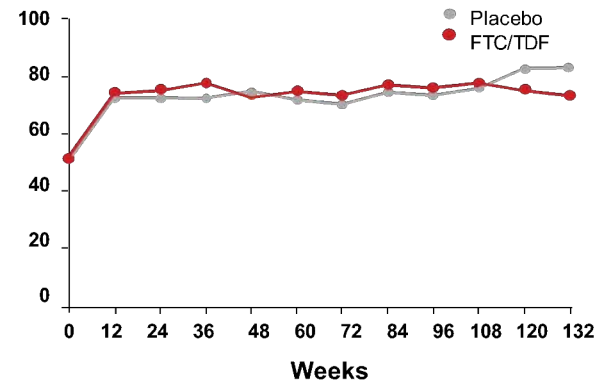
NEJM, Nov 23, 2010

No Evidence of Risk Compensation in PrEP Clinical Trials

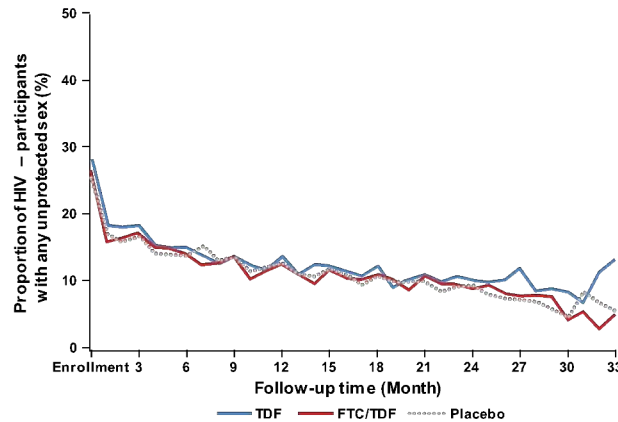
iPrEx^{1,2}



Receptive intercourse using condoms (% of partners)



Partners PrEP³



- In iPrEx, mean number of partners decreased and condom use increased over time^{1,2}
- In Partners PrEP, unprotected sex decreased over time³

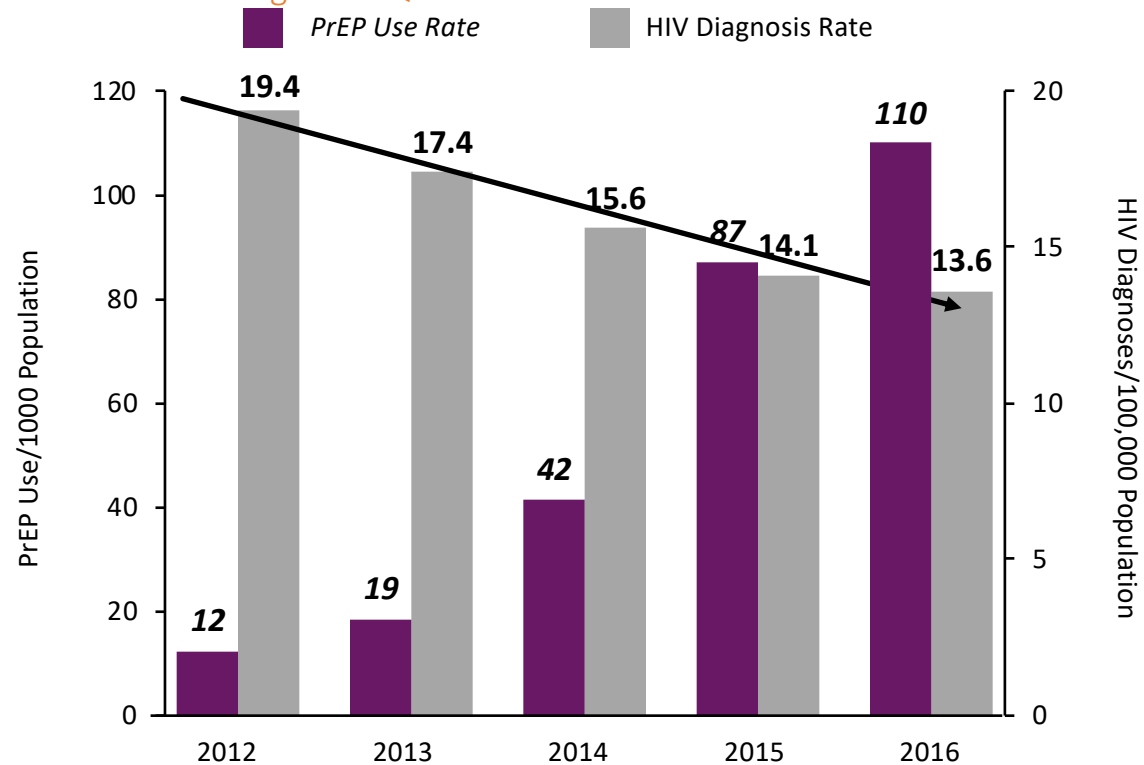
1. Grant R, et al. CROI 2011. Boston. Oral #92
 2. Grant R, et al. N Engl J Med 2010;30:2587-99
 3. Baeten J, et al. IAS 2011; Rome. Oral #MOAX0106

What the data says

PrEP utilization

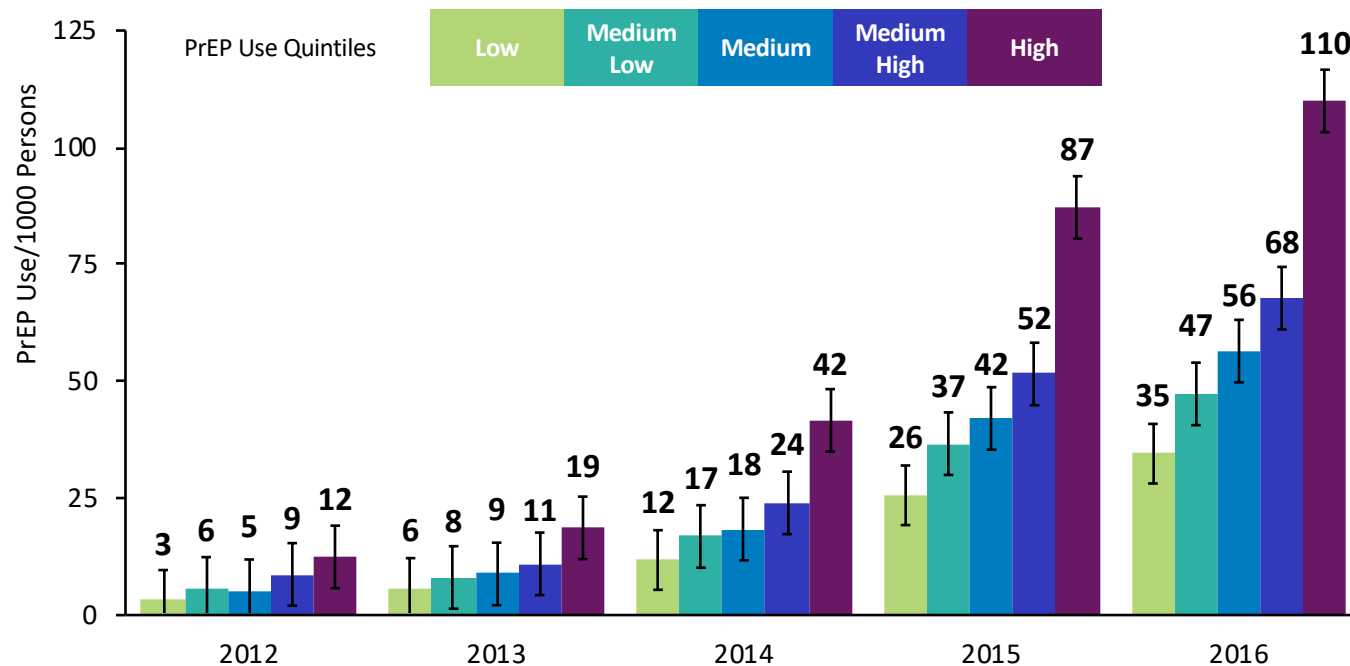
FTC/TDF PrEP Use Rate per 1000 Persons With Indications for PrEP

HIV Diagnosis Rates for US States in High Use Quintile



FTC/TDF PrEP Use Rate per 1000 Persons With Indication for PrEP in States Grouped Into PrEP Use Quintiles and Year

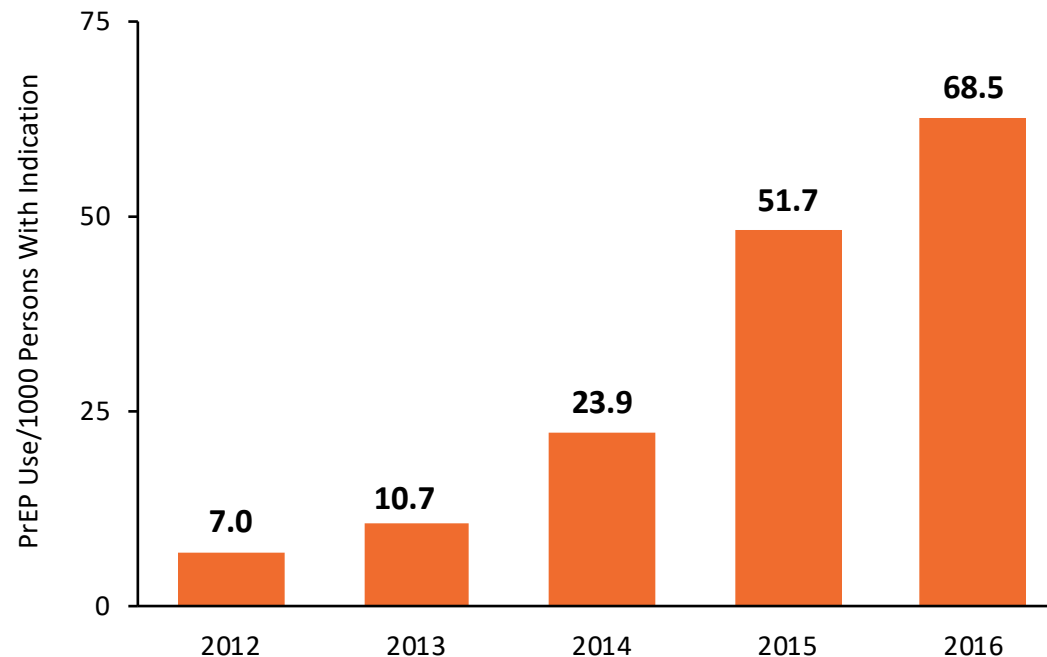
USA 2012–2016



Error bars represent standard error (SE).

National FTC/TDF Use Rate per 1000 Persons with Indication for PrEP

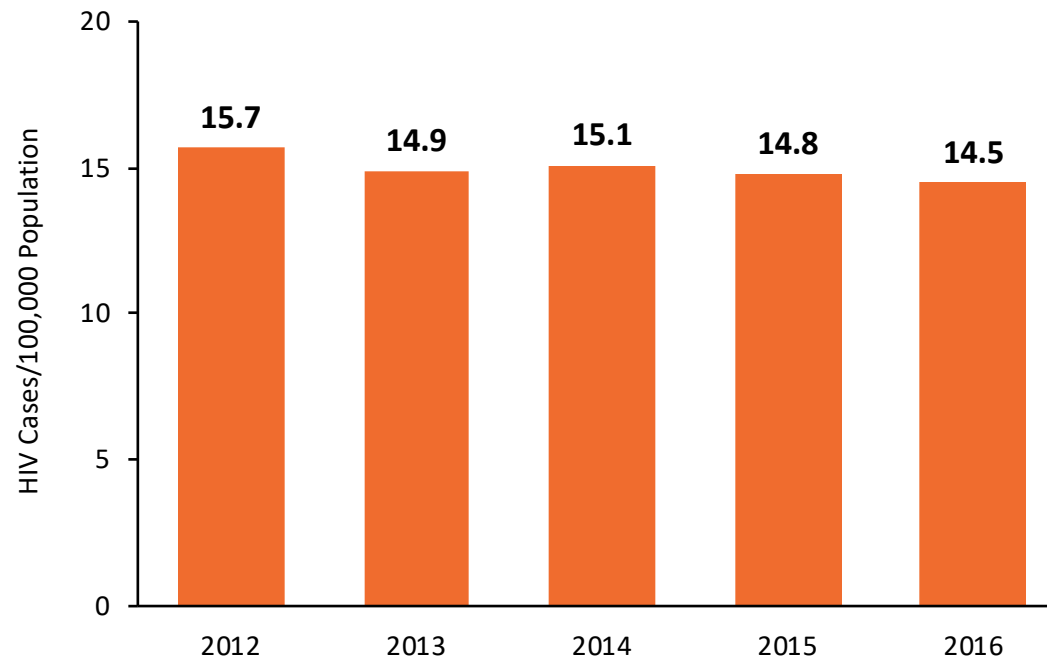
USA 2012–2016



- The national prevalence of FTC/TDF PrEP use increased significantly in the US from 2012 to 2016:
 - 7.0/1000 persons with indication in 2012
 - 68.5/1000 persons with indication in 2016 (EAPC: +78.0%, 95% CI: +77.3, +78.7%)

National HIV Diagnosis Rate in Persons Age ≥ 13 Years per 100,000 Population

USA 2012–2016



- The national rate of HIV diagnoses decreased in the US from 2012 to 2016:
 - 15.7/100K population in 2012
 - 14.5/100K population in 2016 (EAPC -1.6, 95% CI -1.9, -1.3)

2014 USPHS/CDC Guidelines for PrEP: Time to Achieve Steady State Levels of TFV-DP

- The time from initiation of daily oral doses of TRUVADA to maximal protection against HIV infection is unknown
- Data from exploratory pharmacokinetic studies conducted with HIV-uninfected men and women provide preliminary data on the lead-time required to achieve steady state levels of TFV-DP in peripheral blood mononuclear cells, rectal, and vaginal tissues

Daily Oral PrEP: Time to Maximum Intracellular Concentrations of TFV-DP in Different Tissues	
Rectal tissue	~7 days
Blood	~20 days
Cervicovaginal tissues	~20 days
Penile tissues	No data available

TFV-DP, tenofovir diphosphate
US Public Health Services. Preexposure Prophylaxis For The Prevention of HIV Infection In The United States, 2014.
<http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf>

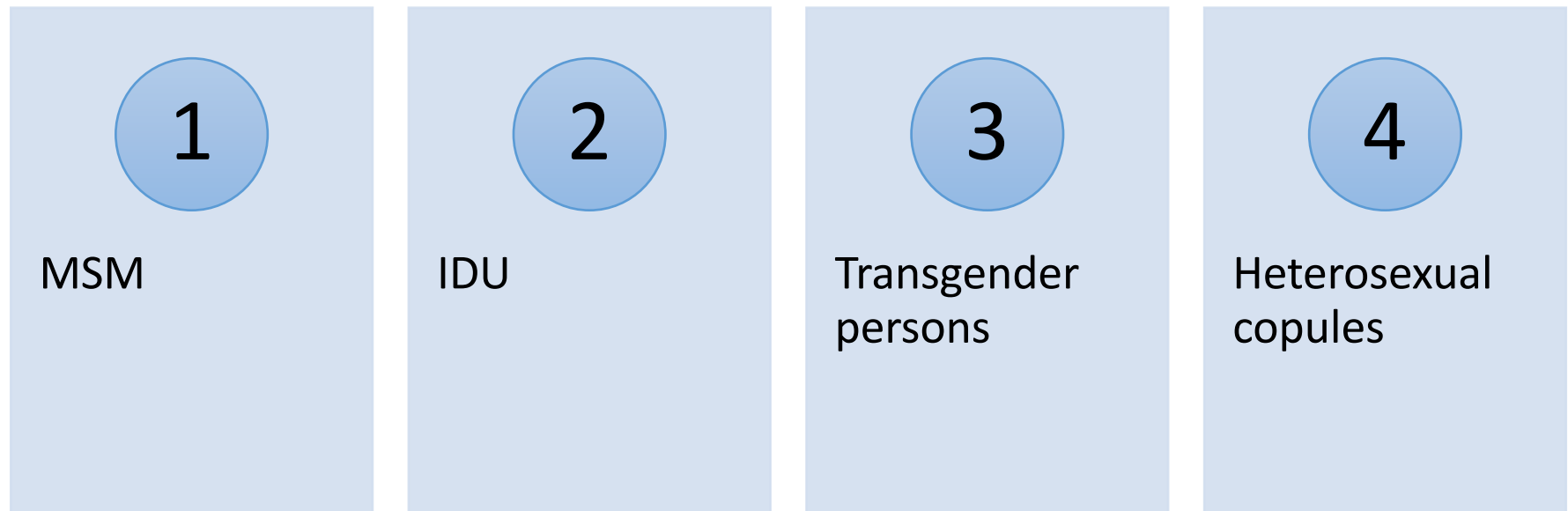
U.S. Preventative Services Task Force

Population	Recommendation	Grade		
Persons at high risk of HIV acquisition	The USPSTF recommends that clinicians offer pre-exposure prophylaxis (PrEP) with effective antiretroviral therapy to persons who are at high risk of HIV acquisition.	A		
		The USPSTF recommends the service. There is high certainty that the net benefit is substantial. Offer or provide this service		

Prescribe HIV Prevention

<https://www.cdc.gov/actagainstaids/campaigns/prescribe-hiv-prevention/index.html>

PrEP Candidates



<http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf>

1

MSM

- Men who have sex with men (MSM)
 - HIV-positive sexual partner
 - Recent bacterial STI
 - High number of sex partners
 - History of inconsistent/no condom use
 - Commercial sex work



HIV Incidence Risk Index for MSM (HIRI-MSM)

- Scored 7-item screening index predicted HIV seroconversion in two large prospective cohorts of MSM in the United States
- Useful to prioritize patients for PrEP and other intensive HIV prevention efforts

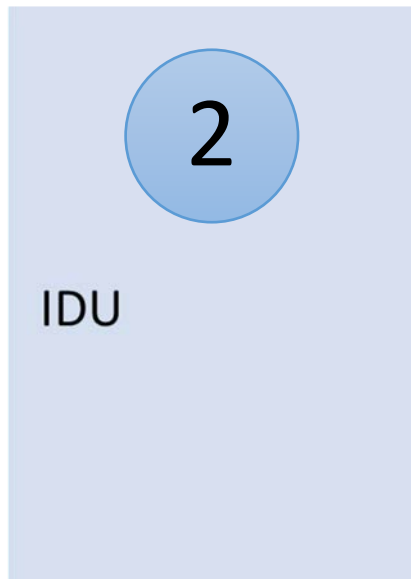
Score	Prevention Tactic
≥10	PrEP evaluation
≤9	Standard prevention

HIRI-MSM Risk Index*			
1.	How old are you today (yrs)?	<18 years	Score 0
		18-28 years	Score 8
		29-40 years	Score 5
		41-48 years	Score 2
		≥ 49 years	Score 0
2.	How many men have you had sex with in the last 6 months?	> 10 male partners	Score 7
		6-10 male partners	Score 4
		0-5 male partners	Score 0
3.	In the last 6 months, how many times did you have receptive anal sex without a condom (you were the bottom) with a man?	1 or more times	Score 10
		0 times	Score 0
4.	How many of your male sex partners were HIV positive?	>1 positive partner	Score 8
		1 positive partner	Score 4
		<1 positive partner	Score 0
5.	In the last 6 months, how many times did you have insertive anal sex (you were the top) with a man who was HIV positive?	5 or more times	Score 6
		0 times	Score 0
6.	In the last 6 months, have you used methamphetamines such as crystal or speed?	Yes	Score 5
		No	Score 0
7.	In the last 6 months, have you used poppers (amyl nitrate)?	Yes	Score 3
		No	Score 0
Add down entries in right column to calculate total score			Total Score†

*To identify sexually active MSM in their practice, we recommend clinicians ask all their male patients a routine question: "In the past (time) have you had sex? (if yes), with men, women, or both?"

† If Score is 10 or greater, evaluate for PrEP or other intensive HIV prevention services. If score is 9 or less, provide indicated standard HIV prevention services.

PrEP: Candidates



- **Injection drug users (IDU)**

- HIV-positive injecting partner
- Sharing injection equipment
- Recent drug treatment (but currently injecting)

PrEP: Candidates



- Engaging in high-risk sexual behaviors
- HIV-positive sexual partner
- Recent bacterial STI
- High number of sex partners
- History of inconsistent/no condom use
- Commercial sex work
- High-prevalence area or network
 - TGW risk

Which Heterosexual Women and Men?



- Those with:
 - High risk of encountering HIV+ partners
 - local/network HIV prevalence
 - Known HIV+ partner (with detectable viral load?)
 - Surrogate markers (e.g., incarceration hx, poverty)
 - Inconsistent or never use of condoms during sex
 - Self-report
 - Surrogate markers (STI hx, unintended pregnancy)

Medication Adherence Counseling

- Address adverse events^[1]
- Identify barriers to adherence^[1]
- Respond to missed doses in nonjudgemental manner, and stress importance of adherence^[1]
- Patient self-reporting may not reflect actual adherence^[2,3]



[This Photo](#) by Unknown Author is licensed under [CC BY-ND](#)

1. CDC. PrEP Guideline. 2014. 2. Van Der Straten A, et al. CROI 2014. Abstract 44. 3. Baxi SM, et al. CROI 2014. Abstract 953.

Stopping PrEP

- PrEP is not meant to be a “permanent” intervention. PrEP should be used during periods of high risk.
- Reasons to stop PrEP:
 - Evidence of HIV infection
 - Adverse events
 - Chronic nonadherence
 - Change in level of risk
 - Patient choice
- If restarting PrEP after stopping, repeat standard pre-PrEP evaluation

CDC. PrEP Guideline. 2014.



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Safety and Tolerability

Adverse Events

- Very few and mild AEs observed in PrEP trials^[1]
 - iPrEx: small but significant early nausea and weight loss^[2]
- Potential bone and renal toxicity
 - Known risk associated with TDF
- Potential for drug-resistant HIV infection
 - Infrequent in clinical trials but must exclude HIV infection



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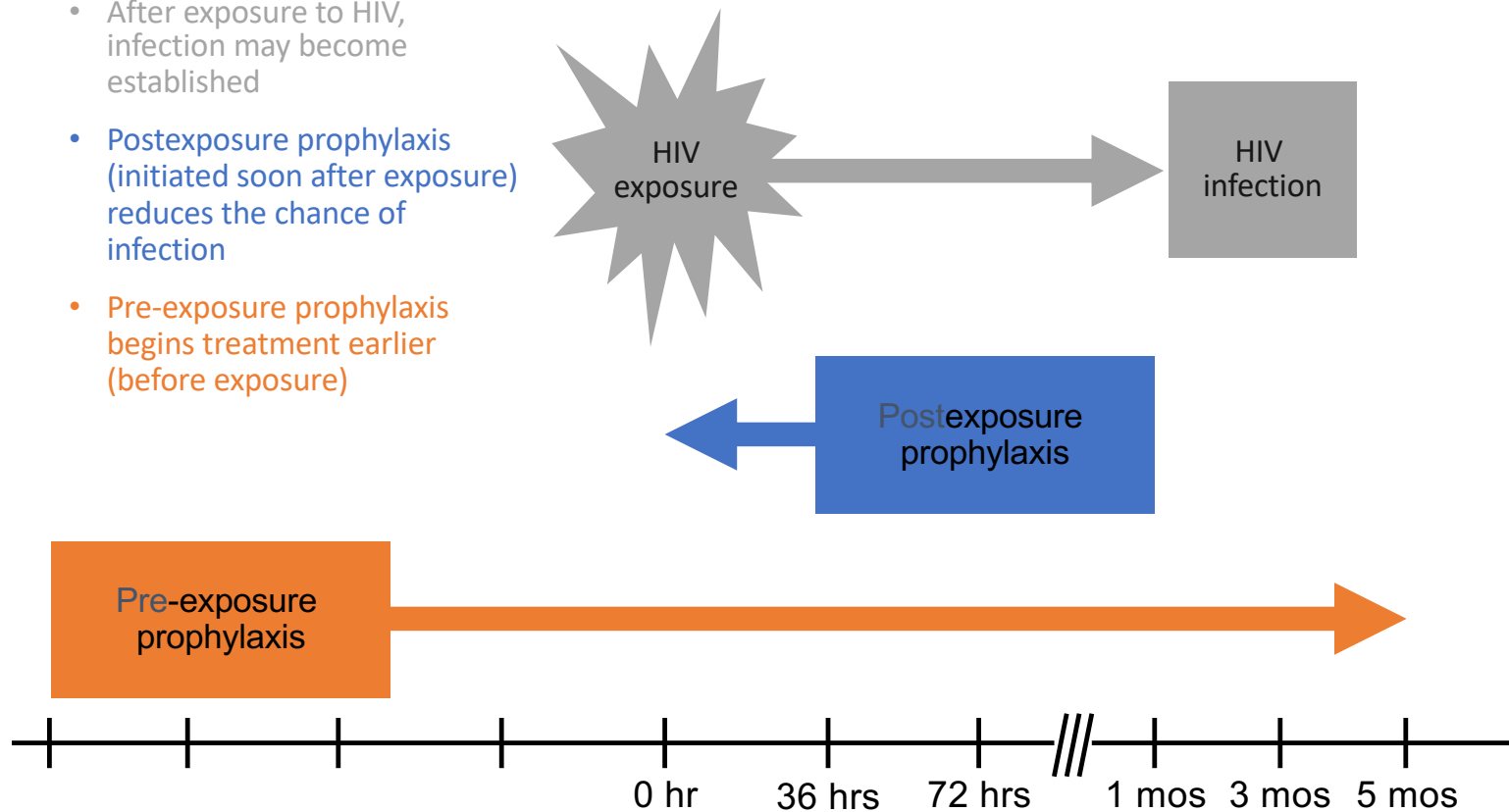
1. CDC. PrEP Guideline. 2014. 2. Grant RM, et al. N Engl J Med. 2010;363:2587-2599.



Post Exposure Prophylaxis

Pre- vs Postexposure 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)



What is PEP?

- Treatment with anti-retroviral drugs
 - Within 72 hours
 - For 28 days
 - Need treatment for other STI's as well

- ALL persons should be considered when care is sought <72 hours
 - Non occupational exposure to HIV
 - Condom break
 - No condom
 - Substantial risk

Who gets
PEP?

Type of exposure	Risk per 100,000 exposures
Blood transfusion with HIV+ blood	9,250
Receptive anal sex (being penetrated by HIV+ partner)	138
Sharing needles with HIV+	63
Insertive anal sex (penetrating an HIV+ partner)	11
Receptive penile-vaginal intercourse (male+)	8
Insertive penile-vaginal intercourse (female+)	4
Receptive oral intercourse from an HIV+ partner	Low
Insertive oral intercourse (performing on HIV+ partner)	Low

HIV acquisition risk

What drugs to use?



Tenofovir TDF with Emtricitabine once daily and Raltegravir 400 mg BID or Dolutegravir 50 mg qd



Alternate

Tenofovir plus darunavir 800 mg and ritonavir 100 mg daily



Other options:

Other single tablet ARV

PEP Testing, treatment and follow up



Testing, at initial visit

HIV, rapid if possible
Hepatitis B, C
STI
?CMP



Treatment

STI as indicated



Follow up

28 days
Evaluation/discussion about transition to PrEP

nPEP or PrEP
to do list:

Acute HIV Infection

- Patients who are candidates for PrEP are at substantial risk of HIV infection
- Acute HIV infection should be suspected in patients with recent HIV exposure^[1]
 - Signs and symptoms include fever, rash, pharyngitis, lymphadenopathy, myalgia, headache, diarrhea, arthralgia^[2]
- All PrEP candidates with a negative or indeterminate HIV antibody test **MUST** be asked about symptoms of viral illness in the previous month or on the day of evaluation
 - Additional confirmatory testing is needed in patients reporting recent signs or symptoms suggestive of acute HIV

1. CDC. PrEP Guideline. 2014.

2. Daar ES, et al. Curr Opin HIV AIDS. 2008;3:10-15.

HIV Screening

- Exclude acute and chronic HIV infection^[1,2]
 - May need to use 4th-generation HIV Ag/Ab or HIV-1 RNA using nucleic acid–based tests if acute infection is suspected
 - Document negative antibody test within the week before starting PrEP
 - Do not accept patient-reported results
 - Avoid use of **oral rapid** HIV testing due to lower sensitivity

1. CDC. PrEP Guideline. 2014.

2. Daar ES, et al. Curr Opin HIV AIDS. 2008;3:10-15.

TasP



Treatment as Prevention

- People living with HIV who take HIV medication daily as prescribed and get and keep an undetectable viral load have effectively no risk of sexually transmitting HIV to their HIV-negative partners. This is called **treatment as prevention** (TasP), using HIV medication to prevent sexual transmission of HIV. It is one of the highly effective options for preventing HIV transmission.
- TasP works when a person living with HIV takes HIV medication exactly as prescribed and has regular follow-up care, including regular viral load tests to ensure their viral load stays undetectable.



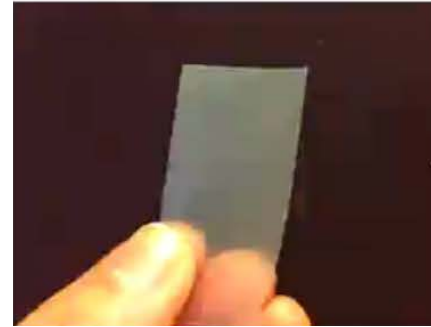
What's Next in PrEP

PrEP for the Future

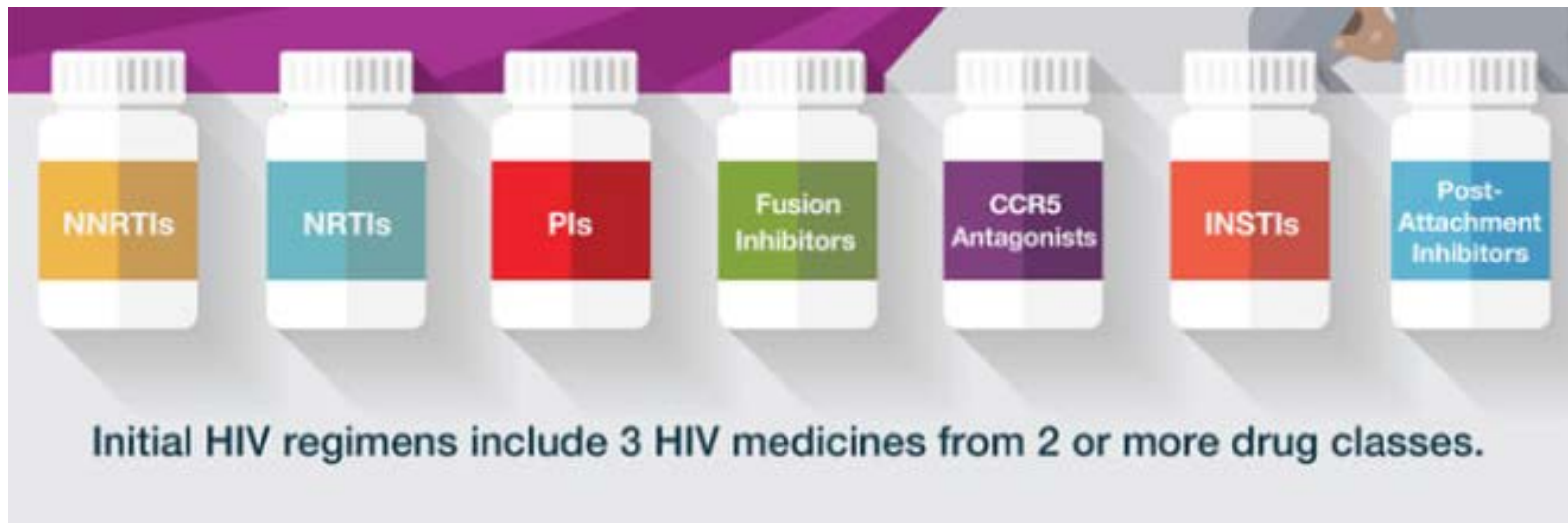
- Subcutaneous TAF implant
- Tenofovir rectal douche on demand
- Cabotegravir long acting injection
- Combination vaginal ring of dapirivine and levonorgestrel for HIV and pregnancy prevention

PrEP in the Future

- Rectal/vaginal gels
- Availability of Tenofovir Alafenamide (TAF) → reduced risk of BMD and renal complications
- New dosing protocols for Truvada and other oral PrEP formulations
- Long-acting injectable PrEP (cabotegravir and rilpivirine injectables animal studies and early human studies very promising)!

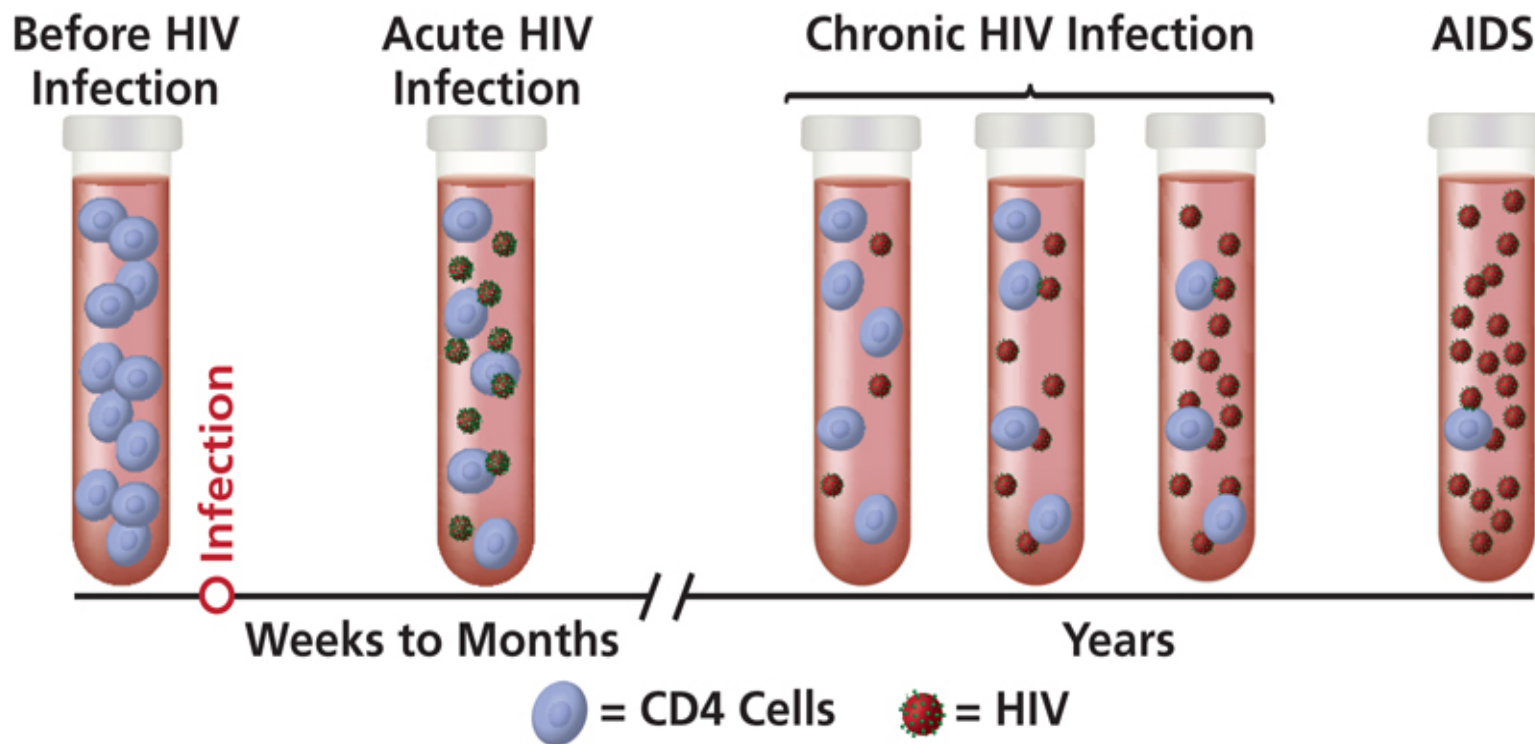


HIV Treatment at a Glance



HIV Progression w/o Treatment

HIV Progression





Treatment Goals

- Maximally and durably suppress plasma HIV RNA
- Restore and preserve immunologic function
- Reduce HIV-associated morbidity and prolong the duration and quality of survival
- Prevent HIV transmission

Drug Classes

- Entry Inhibitors
- Integrase Inhibitors
- Post attachment inhibitor (NEW CLASS – 2018)
- Protease Inhibitors
- Reverse Transcriptase Inhibitors
 - Nucleoside reverse transcriptase inhibitors (NRTI)
 - Nucleotide reverse transcriptase inhibitors (NtRTI)
 - Non-Nucleoside Reverse Transcriptase Inhibitors

Entry Inhibitors

- **Maraviroc (Selzentry®)**
 - Entry Inhibitor
 - Mechanism of Action - Prevents HIV entry into human cells by blocking the CCR5 coreceptor
- **Enfuvirtide (Fuzeon®)**
 - Fusion Inhibitor
 - Synthetic peptide derived from GP41
 - Mechanism of Action - Prevents fusion of HIV and human cell membranes thus preventing entry into human cells
- **Clinical Pearls**
 - Requires viral tropism testing prior to therapy initiation
 - Determine which coreceptor is used by virus to enter cells
 - CCR5 or CXCR4 or both
 - Mixed tropism associated with decreased response to therapy

Integrase Inhibitors

- **Available Agents**

- Bictagravir *Used in combination with Biktarvy®
- Dolutegravir (Tivicay®)*Used in combination for Triumeq®
- Raltegravir (Isentress®)
- Elvitegravir (Vitekta®) *Used in combination product Stribild® and Genvoya®

- **Mechanism of Action**

- Integrase is an enzyme which allows the proviral DNA strand to be incorporated into the host cell DNA and is needed for viral multiplication
- By inhibiting integrase, Raltegravir and Elraltegravir prevents unintegrated HIV DNA into host cell genome preventing formation of HIV provirus

- **Clinical Pearls**

- Twice daily dosing with Raltegravir (Isentress®)
- Do not use with Rifampin

Post Attachment Inhibitor

- Ibalizumab (Trogarzo®)
- Mechanism of Action
 - Recombinant humanized monoclonal antibody CD-4 directed post-attachment HIV-1 inhibitor
- Indication
 - Treatment of HIV-1 in heavily treatment-experienced adults with multidrug resistant HIV-1 infection failing other antiretroviral regimen
- Dosing
 - IV infusion given over 15 to 30 minutes
 - Every 2 weeks
- Adverse effects
 - Risk of immune reconstitution inflammatory syndrome (IRIS)
 - Nausea, occasional dizziness, diarrhea, and rash



 **NEW**
Trogarzo™
(ibalizumab-uiyk)
Injection
200 mg/1.33 mL (150 mg/mL)

Protease Inhibitors

- **Available Products (un-boosted)**

- Atazanavir (Reyataz®)
- Darunavir (Prezista®) *Available as a fixed dose combination boosted with cobicistat + emtricitabine and tenofovir alafenamide (Descovy®)
 - Darunavir/cobicistat + emtricitabine and tenofovir alafenamide (Symtuza®)
- Boosting Agents
 - Ritonavir (Norvir®)
 - Cobicistat *Used in combination products

- **Mechanism of Action**

- Inhibit HIV type I aspartate protease (enzyme involved in HIV replication)
- Exert effect on latter stages of HIV life cycle which involve post-translational modifications
- Leads to the production of non-infectious, immature HIV particles

- **Clinical Pearl**

- MOST likely ART to cause drug interactions due to CYP-450 system induction

Reverse Transcriptase inhibitors

- **Available Products**

- NRTI - Abacavir (Ziagen®), Emtricitabine (Emtriva®), Lamivudine (Epivir®)

- **Mechanism of Action**

- Inhibit “Reverse Transcriptase”, which is the enzyme that enables viral DNA to be synthesized from human genome
- Preventing the incorporation of HIV genetic material into cellular genetic material

- **Available Products**

- NtRTI – tenofovir disoproxil fumarate (TDF - Viread®)
- NtRTI – tenofovir alafenamide (TAF)

- **Mechanism of Action**

- Acyclic nucleoside phosphonate (nucleotide) diester analog of adenosine monophosphate
- Nucleotide Reverse Transcriptase Inhibitors, also commonly referred to as “tides”, require two phosphorylations to become incorporated into DNA material

Reverse Transcriptase inhibitors

- **Available Products**

- NNRTI - Efavirenz (Sustiva®), *Rilpivirine (Edurant®), *Doravirine (Pifeltro®)
- New Agent August 2018 - *Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate (combo product – Delstrigo®)

- **Mechanism of Action**

- These inhibit the Reverse Transcriptase enzyme without actually becoming incorporated into the DNA chain
- *Better resistance profile

Combination ART Products

Co-formulated Fixed Dose Combinations

Single Tablet Regimens

- Abacavir/Lamuvudine (ABC/3TC) – Epzicom®
- Atazanvir/cobicistat (ATV/c) – Evotaz®
- Bictegravir/Emtricitabine/Tenofovir AF (Biktarvy®)
- Darunavir/cobicistat (DRV/c) – Prezcoibx®
- Darunavir/cobicistat/Emtricitabine/Tenofovir AF (Symtuza®)
- *Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate (Delstrigo®)*
- Dolutegravir/Abacavir/Lamuvudine (DTG/ABC/3TC) – Triumeq®
- Efavirenz/Tenofovir DF/Emtricitabine (EFV/TDF/FTC) – Atripla®
- Elvitegravir/cobicistat/Tenofovir DF/Emtricitabine (EVG/c/TDF/FTC) – Stribild®
- Elvitegravir/cobicistat/Tenofovir AF/Emtricitabine (EVG/c/TAF/FTC) – Genvoya®
- *Lopinavir/ritonavir (LPV/r) – Kaletra®*
**NO LONGER RECOMMENDED*
- Rilpivirine/Tenofovir DF/Emtricitabine (RPV/TDF/FTC) – Complera®
- Rilpivirine/Tenofovir AF/Emtricitabine (RPV/TAF/FTC) – Odefsey®
- Tenofovir DF/Emtricitabine (TDF/FTC) – Truvada®
- Tenofovir AF/Emtricitabine (TAF/FTC) – Descovy®
- ***Dolutegravir/Rilivirine (Juluca®) used for switch therapy

Adverse Effects – By drug class

➤ **Entry Inhibitors**

- Abdominal pain, Cough, Dizziness, musculoskeletal symptoms, rash, URIs, orthostatic hypotension
- Hepatotoxicity (Black Box Warning-Maraviroc®)
- Injection site reaction, hypersensitivity reaction (Fuzeon®)

➤ **Integrase Inhibitors**

- Nausea, diarrhea, headache, rash, pyrexia, hyperglycemia, increased LFTs
- Myopathy, creatinine kinase, rhabdomyolysis
- Lipodystrophy, Elevated CPK, muscle weakness

- Protease Inhibitors
 - Dyslipidemia, GI disturbances (mainly diarrhea), N/V, Hepatotoxicity, Insulin Resistance, Lipodystrophy
 - Increased risk of bleeding
- Nucleoside Reverse Transcriptase Inhibitors
 - Headaches, Lactic Acidosis, Lipoatrophy, Mitochondrial Dysfunction
 - Nausea, Vomiting
 - Hepatomegaly w/steatosis

Adverse
Effects – By
drug class

➤ **Nucleotide Reverse Transcriptase Inhibitors**

- CrCl < 50 mL/min? dosing adjustment (TDF) - Fanconi Syndrome
 - CrCl < 30 mL/min (contraindication for TAF)
- Renal insufficiency, Headache, Diarrhea, asthenia, decrease bone mineral density (BMD)

➤ **Non Nucleoside Reverse Transcriptase Inhibitors**

- BBW for liver toxicity (Nevirapine®)
- Hepatic issues
- Many drug Interactions
- Neuropsychiatric effects (Efavirenz®)
- Rash, and severe skin reactions (SJS and TEN) have occurred but rare
- Decreased BMD with co-administration NRTI and PIs

Adverse
Effects – By
drug class

	ART Initiation	2 to 8 weeks after ART initiation or modification	Every 3 to 6 months	Every 6 months	Every 12 months	Treatment Failure	If ART Initiation is Delayed
CD4 Count	✓		✓ (during the first 2 years or viremia develops)		✓ (after 2 years with consistent suppressed viral load)	✓	✓ (every 3-6 months)
HIV Viral Load	✓	✓	✓	✓		✓	✓ Repeat testing is optional
Basic Chemistry	✓	✓	✓				✓ Every 6-12 months
ALT, AST, T. Bilirubin	✓	✓	✓				✓ Every 6-12 months
CBC w/Diff	✓		✓ *if CD4 testing is done	✓			✓ Every 3-6 months
Fasting Lipid Profile	✓			✓ If abnormal at last test	✓ If abnormal at last test		✓ If normal at baseline, annually
Fasting Glucose or HbA1c	✓		✓ If abnormal at last test		✓ If abnormal at last test		✓ If normal at baseline, annually
Urinalysis	✓			✓ If on TDF	✓		✓ If normal at baseline, annually

Laboratory Monitoring

DHHS Guideline Recommendations

- Treatment Naïve – Recommended Regimens for MOST people with HIV
- INSTI-Based Regimens
 - Bictegravir/tenofovir AF/Emtricitabine (Biktarvy®)
 - Dolutegravir/Abacavir/Lamuvudine (DTG/ABC/3TC) Triumeq® - only for patients who are HLA-B*5701 negative (hypersensitivity reaction) (AI)
 - Dolutegravir (Tivicay®)(DTG) plus either Tenofovir DF/Emtricitabine (Truvada®)(TDF/FTC) OR **Tenofovir AF/Emtricitabine (Descovy®) (TAF/FTC)** (AI)
 - Elvitegravir/cobicistat/Tenofovir AF/Emtricitabine (EVG/c/TAF/FTC) Genvoya® – only for patients with pre-treatment estimated CrCl ≥30 mL/min (AI)
 - Elvitegravir/cobicistat/Tenofovir DF/Emtricitabine (EVG/c/TDF/FTC) Stribild® – only for patients with pre-treatment estimated CrCl ≥70 mL/min (AI)
 - Raltegravir (Isentress®)(RAL) plus either Tenofovir DF/Emtricitabine (Truvada®)(TDF/FTC) OR **Tenofovir AF/Emtricitabine (Descovy®) (TAF/FTC)** (AI)

- Recommended Initial Regimens in Certain Clinical Situations
 - Boosted PI-Based Regimens
 - ATV/c (Evotaz®) or ATV/r plus either TDF/FTC (Truvada®) or **TAF/FTC (Descovy®)** - only for patient with pre-treatment estimated CrCl \geq 70 mL/min (BI)
 - ATV/r plus TDF/FTC (Truvada®) (BI)
 - DRV/c (Prezcobix®) (BIII) or DRV/r (BII) plus ABC/3TC (Epzicom®) – only for patient who are HLA-B*5701 negative
 - DRV/c (Prezcobix®) plus either TDF/FTC (Truvada®) or **TAF/FTC (Descovy®)** - only for patient with pre-treatment estimated CrCl \geq 70 mL/min (BII)

DHHS Guideline Recommendations

DHHS Guideline Recommendations

- Treatment Naïve - Recommended Initial Regimens in Certain Clinical Situations
 - NNRTI-Based Regimens
 - EFV/TDF/FTC* (BI)
 - EFV plus TAF/FTC (BII)
 - RPV/TDF/FTC (Complera®) or RPV/TAF/FTC (Odefsey®) - only for patients with pre-treatment RNA < 100,000 copies/mL and CD4 count > 200 cells/mm³ (BI)
- Regimens to Consider when ABC, TAF, and TDF Cannot be Used:
 - DRV/r + RAL (BID) (CI)—if HIV RNA 200 cells/mm³
 - LPV/r + 3TCa (BID)e (CI)

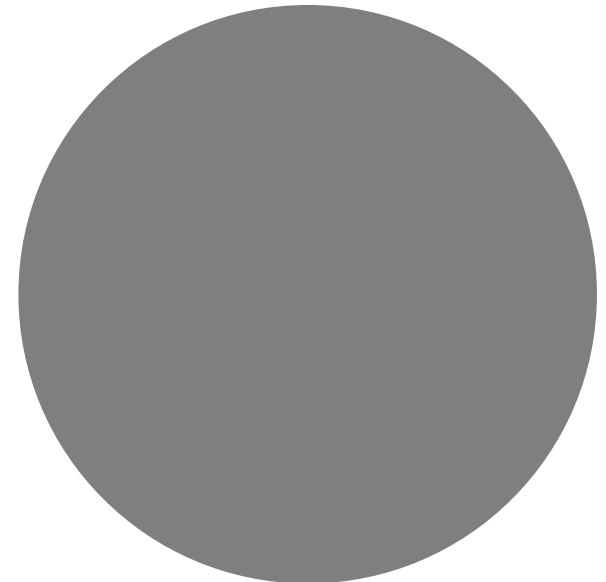
- Treatment Experienced Classifications
 - Virologic failure
 - Poor CD4 Cell Recovery and Persistent Inflammation Despite viral suppression
 - Discontinuation or Interruption of Antiretroviral Therapy
- Antiretroviral Considerations in Special Populations (separate section of the guidelines)
 - Acute or Recent (Early) HIV Infection
 - HIV-Infected Children*
 - HIV and Illicit Drug Users
 - HIV-Infected Women*
 - HIV-2 Infection *
 - HIV and the Older Patient

***Separate Guidelines**

DHHS Guideline Recommendations

- CrCl \leq 70ml/min
 - Elvitegravir/cobicistat/Tenofovir DF/Emtricitabine (EVG/c/TDF/FTC) – Stribild® **CONTRAINDICATED**
- CrCl \leq 30ml/min
 - Elvitegravir/cobicistat/Tenofovir AF/Emtricitabine (EVG/c/TAF/FTC) – Genvoya® **CONTRAINDICATED**
- HLA-B*5701 positive (hypersensitivity reaction)
 - Dolutegravir/Abacavir/Lamuvudine (DTG/ABC/3TC) Triumeq® **CONTRAINDICATED**
- Viral load > 100,000 copies/ml or CD4 count < 200cell/mm³
 - Rilpivirine/emtricitabine/tenofovir disoproxil fumarate (Complera®) OR Rilpivirine/emtricitabine/tenofovir alafenamide (Odesfsey®) **CONTRAINDICATED**

Special Considerations



- Since RPV-containing STRs are smaller in size than other STRs, they may be considered when a person has difficulty swallowing a larger pill
- ARV can be started before HIV drug resistance results are available (Rapid Initiation)
 - DRV/r or DRV/c + tenofovir/FTC
 - or
 - DTG + tenofovir/FTC
 - or
 - Bictegravir/tenofovir/FTC
 - Avoid NNRTI based regimens

Special Considerations



Conclusions/Recommendations



PrEP Works!



Most efficacious if we coordinate our efforts in the community



We all have a role to play: public health officials, community activists, educators, providers.



Don't forget other pillars of prevention:

HIV Testing that adheres to CDC/USPTF guidelines

Treatment as Prevention

PEP



Provider education and buy-in is key



Raise awareness in the community to increase uptake and reduce stigma



HIV Treatment works



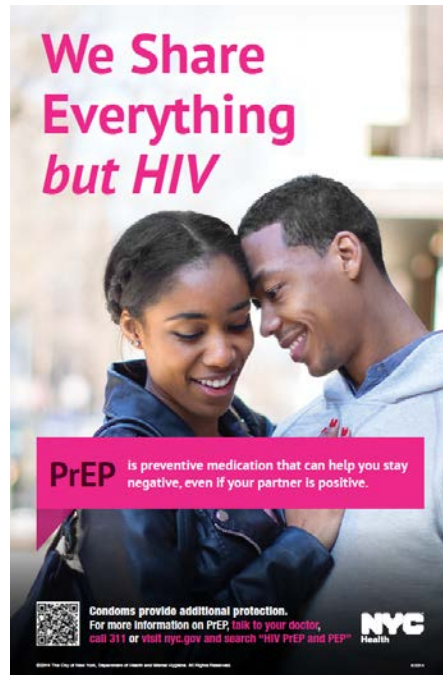
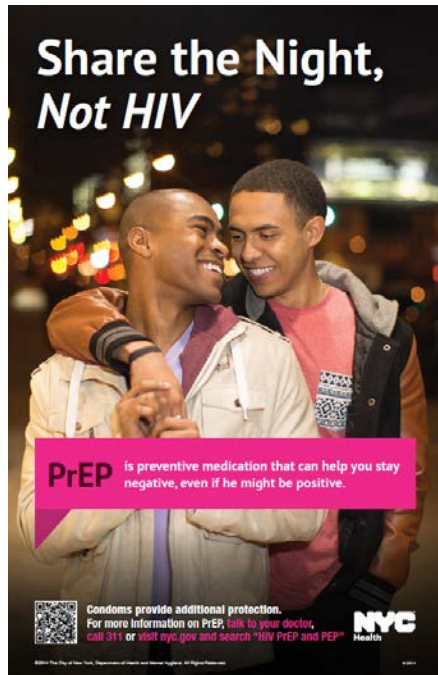
Get patients linked to care whether it's for treatment or prevention early to help stop new infections

References

- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. Department of Health and Human Services. Available at <http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>
- www.aidsinfo.nih.gov
- www.cdc.gov/HIV
- www.lexicomp.com
- www.thomsonsmicromedex.com



Resources



NYC DOH PrEP Posters

Recommendations for PrEP Implementation



Coordinated effort to educate potential users



Visible marketing campaign needed



Need to engage and educate providers



PrEP works in a continuum with PEP and HIV testing



Increase education and availability of PEP



Promote HIV testing in adherence with CDC guidelines
(opt out, universal for all 13-64, no pre-test counseling)



Antiretroviral Pregnancy Registry

- www.apregistry.com
- Collects data on ARV use during pregnancy
 - Treatment or prophylaxis
- Congenital anomalies among 1st trimester prospective reports
 - TDF: 31/1370 2.3% (1.5%, 3.2%)
 - FTC: 21/899 2.3% (1.4%, 3.5%)
 - MACDP (CDC surveillance system, metropolitan Atlanta region) 2.72 per 100 live births

Resources



CDC PrEP website

<http://www.cdc.gov/hiv/prep/>



ACOG

HIV information for OB-GYNs and their patients

<http://www.womenandhiv.org>



**National Perinatal HIV
Hotline/NCCC**

1-888-448-8765

http://www.nccc.ucsf.edu/about_nccc/perinatal_hotline/

Resources



Bay Area Perinatal AIDS Center (BAPAC)

PRO-Men; ovulation prediction videos, PrEP
handout

<http://hiv.ucsf.edu/care/perinatal.html>



AETC-National Resource Center

Trainer and clinician resources

<http://www.aids-etc.org/>



FXB Center

Clinician support tools, including the *HIV and
Preconception Care Toolkit*

<http://www.fxbcenter.org/resources.html>

Resources

- AVAC
 - A global source for updates, advocacy and information on biomedical HIV prevention.
 - <http://www.avac.org/>
- Sister Love
 - A reproductive justice organization for women, with an emphasis on HIV/AIDS.
 - <http://sisterlove.org/>
- The Well Project
 - Health resources for women diagnosed with HIV and AIDS.
 - http://www.thewellproject.org/en_US/
- WORLD
 - Women organized to respond to life-threatening disease
 - <http://www.womenhiv.org/>



PrEP FACTS

People on PrEP should take the medication and do one or more of the following, as directed, to reduce their risk of HIV:

- Consistently use male condoms or female condoms.
- Reduce overall number of sexual partners.
- Get tested regularly for HIV and other STDs and encourage sexual partners to get tested.
- Talk openly and honestly with sexual partners about HIV status and about past and present sexual risks.

What happens if you forget to wear a condom or miss a pill?

- Forgetting to use a condom can increase your risk.
- Missing a pill can lower the drug's chance of working properly.

PrEP

Guidelines from NYSDOH:

Or simply type the following URL into your browser:
www.health.ny.gov/diseases/aids/general/pep/



Contact information for all agencies participating in PrEP pilot:

Trillium Health
259 Monroe Avenue
Rochester, NY 14607
(585) 545-7200

Health & Education Alternatives for Teens (HEAT Program)
760 Parkside Ave., Room 308
Brooklyn, NY 11226
(718) 467-4446

APICHA Community Health Center
70 Walker Street,
New York, NY 10013
(212) 334-6029

HOME (Helping Our Members Evolve)
289 St. Nicholas Ave.
(Between 124th & 125th)
New York, NY 10032
(646) 216-3266

Evergreen Health Services
206 South Elmwood Avenue
Buffalo, NY 14201
(716) 847-0328

William F. Ryan Community Health Network
110 West 97th Street
New York, NY 10025
(multiple clinic locations across Network)
Confidential PrEP hotline:
(212) 484-5813

Truvada is a FDA approved method for Pre-Exposure Prophylaxis that may also be available at other clinics and private practitioners around New York State.



Are you **worried** about getting HIV?

PrEP
can help.



WHAT IS PEP?

PEP (post-exposure prophylaxis) is medicine that you can take if you are HIV-negative and you believe you have just been exposed to HIV. If you take PEP as directed, it can stop the HIV virus from infecting your body.

Do not delay. You need to take PEP as soon as possible after the exposure.

I MIGHT HAVE BEEN EXPOSED TO HIV... WHAT SHOULD I DO?

Exposure to HIV is a Medical Emergency.
You may be able to stop the infection by taking PEP.

NEW YORK STATE DEPARTMENT OF HEALTH
AND THE NEW YORK CITY DEPARTMENT OF
HEALTH AND MENTAL HYGIENE

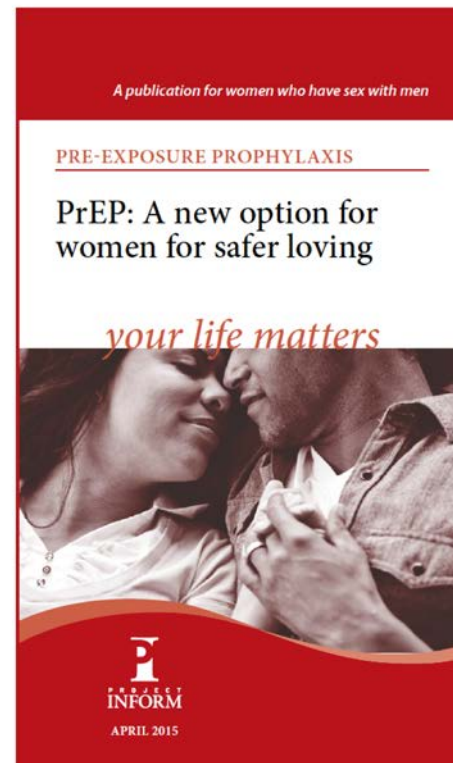
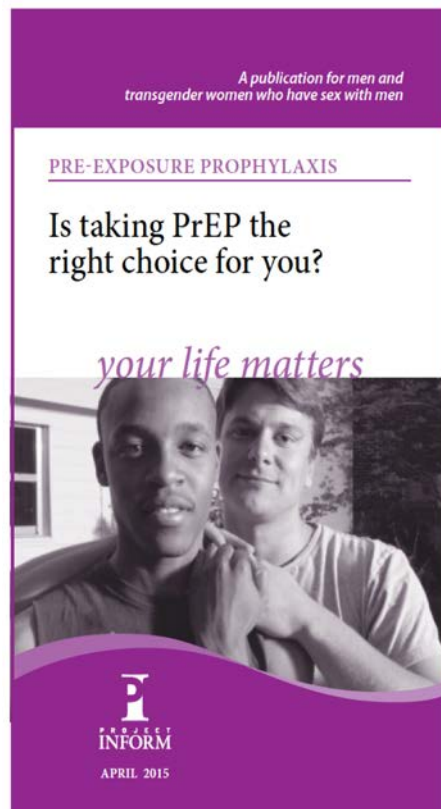


Save this information to your mobile device in case of emergency.

www.hivguidelines.org/what-is-peg

Resources

Educational Materials: Pamphlets



Projectinform.org

Thank you !