

# CDC PUBLIC HEALTH GRAND ROUNDS

## Pre-exposure Prophylaxis (PrEP) for Prevention of HIV Infection



Accessible Version: [https://youtu.be/R6Saff\\_u-xY](https://youtu.be/R6Saff_u-xY)

**May 20, 2014**



U.S. Department of  
Health and Human Services  
Centers for Disease  
Control and Prevention

# HIV Pre-exposure Prophylaxis: Preclinical Research in Animal Models



**Walid Heneine, PhD**

*Surveillance, Antiretroviral Prophylaxis and  
Drug Resistance Team Lead*

Laboratory Branch, Division of HIV/AIDS Prevention  
NCHHSTP



U.S. Department of  
Health and Human Services  
Centers for Disease  
Control and Prevention

# Importance of Animal Models to Assess PrEP Efficacy

- ❑ **Provide first *in vivo* evidence of protection from infection**
  
- ❑ **Assess relationship between efficacy and pharmacologic parameters**
  - How well the drug prevents infection
  - How drugs are distributed systemically
  - How drugs are distributed at mucosal sites of HIV entry (e.g. vaginal, rectal tissue)

# Importance of Animal Models to Assess PrEP Efficacy

- ❑ **Help inform clinical trial designs in humans**
  - Prioritization of PrEP regimens
  - Dose selection
  
- ❑ **Identify most promising PrEP candidates for clinical trials in humans**
  - ~\$20-80 million
  - ~3-5 years to provide answers

# CDC Repeat Exposure Macaque Models

## ❑ Repeat Exposure Macaque Model

- Macaques – preferred animal model for HIV infection
- Virus used - simian HIV (SIV or SHIV)
- Weekly rectal or vaginal exposure to SHIV
- SHIV dose within upper range of HIV infectious dose in humans

## ❑ Exposures to virus repeated to mimic high-risk human exposures to HIV

- Better simulate HIV exposures in humans than do previous models with single high-dose virus challenge
- Protection evaluated against multiple exposure events

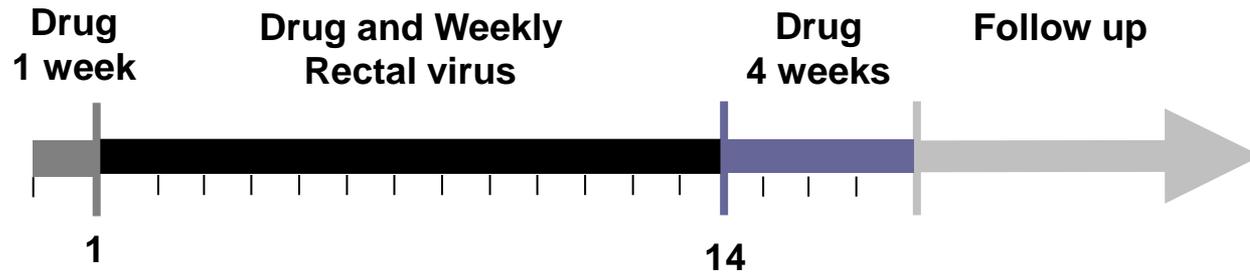
# CDC Repeat Exposure Macaque Models (cont.)

- ❑ **Protection measured over multiple exposures per animal**
  - Power to detect protective effect using smaller numbers of study animals
- ❑ **PrEP regimens that are equivalent to clinical drug exposures in humans**
- ❑ **Inform potential PrEP efficacy trials in humans**

# Drug Selection for PrEP

- ❑ **Among marketed antiretroviral drugs for treatment of HIV-1 infected persons, tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) considered because:**
  - Safe, well tolerated, and potent
  - Reverse transcriptase inhibitors
  - Co-formulated as single once-daily pill marketed as Truvada®
  - Have long plasma (10 to 17 hours) and intracellular (40 to  $\geq 60$  hours) half-lives
    - Long half-life allows forgiveness for imperfect daily use
  - Have even higher penetration in vaginal and rectal tissues

# Design of PrEP Efficacy Study in Animals



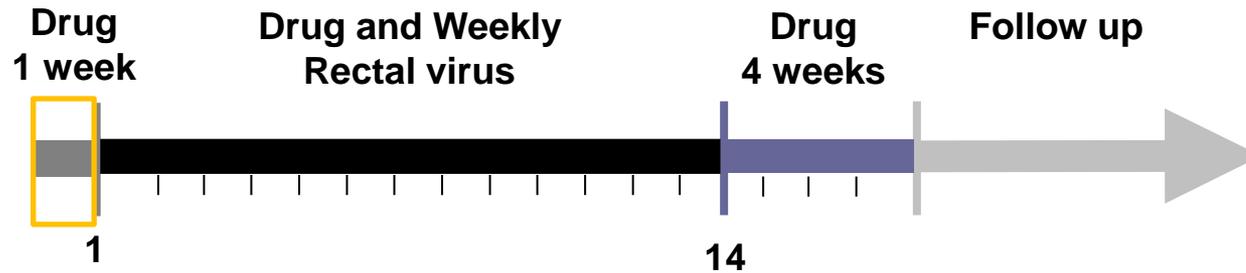
Group 1 (n = 18)  
Untreated controls

Group 2 (n = 6)  
Daily oral TDF and FTC

Group 3 (n = 6)  
Daily subcutaneous FTC and high-dose tenofovir

Group 4 (n = 6)  
Daily subcutaneous FTC

# Design of PrEP Efficacy Study in Animals



**Group 1 (n = 18)**  
Untreated controls

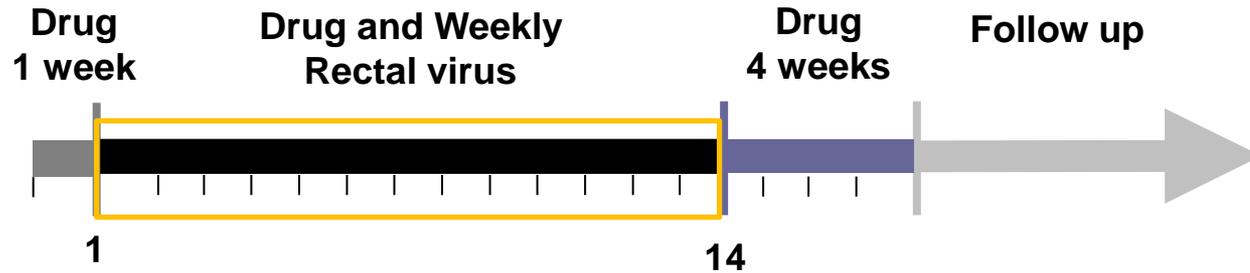
**Group 2 (n = 6)**  
Daily oral TDF and FTC

**Group 3 (n = 6)**  
Daily subcutaneous FTC and high-dose tenofovir

**Group 4 (n = 6)**  
Daily subcutaneous FTC



# Design of PrEP Efficacy Study in Animals



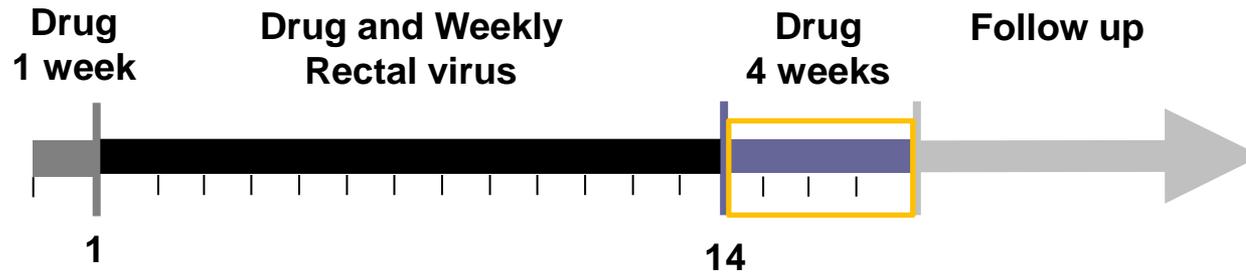
Group 1 (n = 18)  
Untreated controls

Group 2 (n = 6)  
Daily oral TDF and FTC

Group 3 (n = 6)  
Daily subcutaneous FTC and high-dose tenofovir

Group 4 (n = 6)  
Daily subcutaneous FTC

# Design of PrEP Efficacy Study in Animals



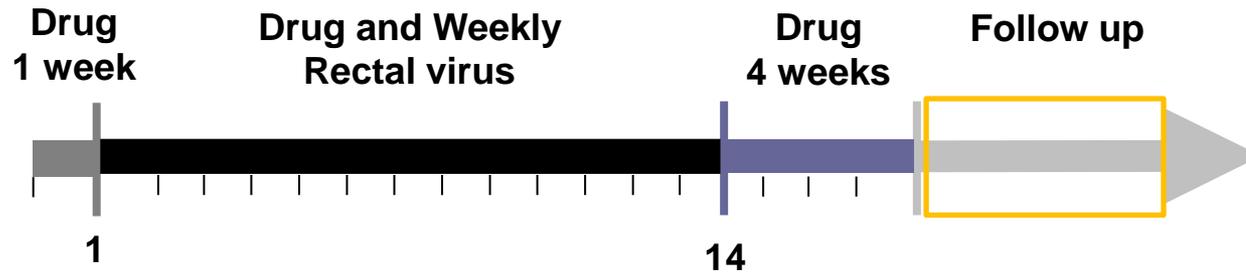
Group 1 (n = 18)  
Untreated controls

Group 2 (n = 6)  
Daily oral TDF and FTC

Group 3 (n = 6)  
Daily subcutaneous FTC and high-dose tenofovir

Group 4 (n = 6)  
Daily subcutaneous FTC

# Design of PrEP Efficacy Study in Animals



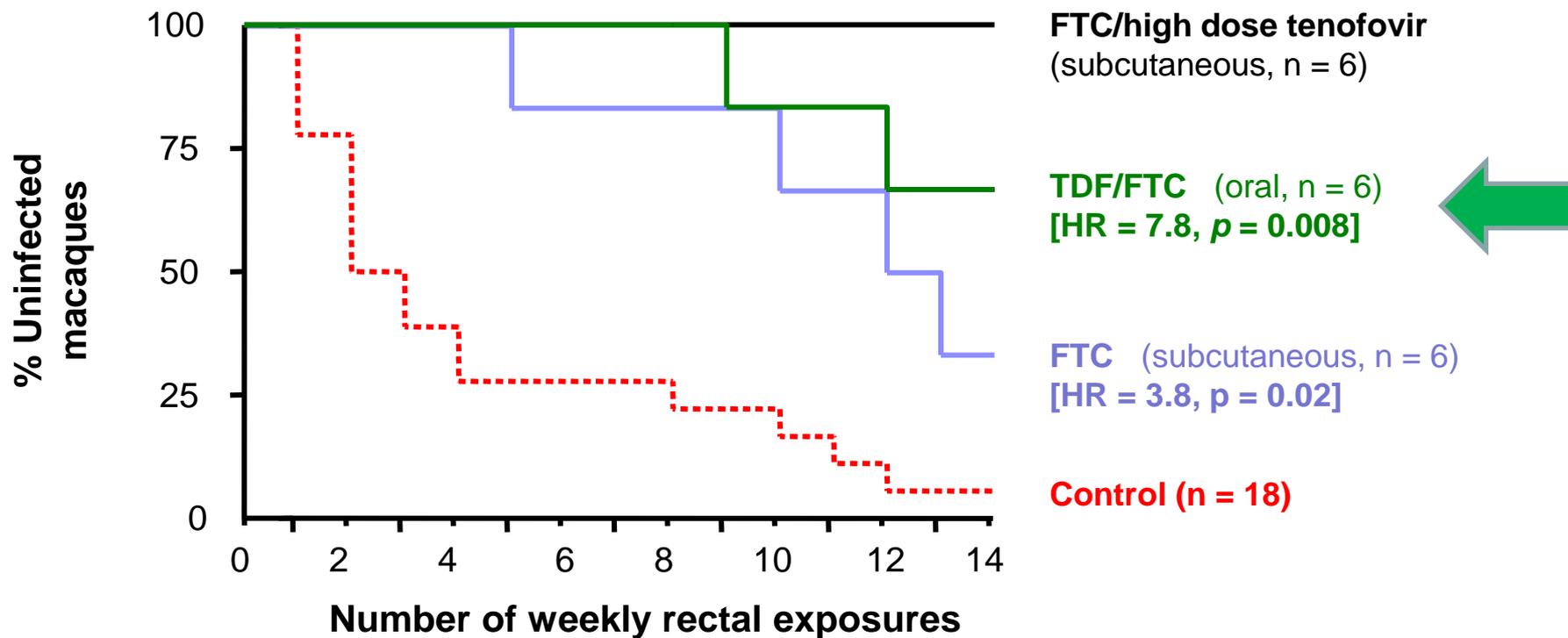
Group 1 (n = 18)  
Untreated controls

Group 2 (n = 6)  
Daily oral TDF and FTC

Group 3 (n = 6)  
Daily subcutaneous FTC and high-dose tenofovir

Group 4 (n = 6)  
Daily subcutaneous FTC

# Daily PrEP Regimens Against Rectal SHIV in Macaques



Garcia-Lerma et al. PLoS Med 2008

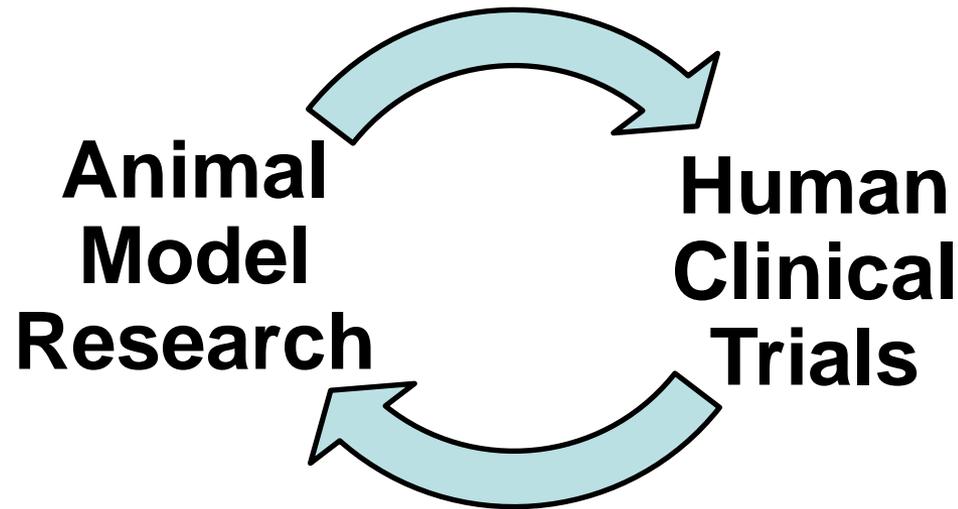
HR: Hazard ratio

TDF/FTC: tenofovir disoproxil fumarate and emtricitabine

# Interpretation and Implications of Animal PrEP Efficacy Study

- ❑ **Daily oral TDF/FTC provided substantial protection against rectal infection**
  - Substantial reduction among oral TDF/FTC-treated compared to control animals
- ❑ **Data informed advancement of oral PrEP into clinical trials in humans**

# Animal and Human PrEP Research



- ❑ **Rectal and vaginal protection**
- ❑ **Drug dose and delivery modality**
- ❑ **Single drug and drug combinations**

# Evolving Evidence from Clinical Trials of HIV Pre-exposure Prophylaxis



**Melanie Thompson, MD**  
*Principal Investigator*  
AIDS Research Consortium of Atlanta



**ARCA**

AIDS Research Consortium of Atlanta  
*Working Together For a Cure*



U.S. Department of  
Health and Human Services  
Centers for Disease  
Control and Prevention

# Disclosures

- ❑ **All research funding is for clinical trials through AIDS Research Consortium of Atlanta; no funding paid directly to Dr. Thompson**
- ❑ **Site Principal Investigator for clinical trials from the following sponsors:**
  - Bristol Myers Squibb, Inc., Cepheid, Inc., Gilead Sciences, GeoVax, Inc., Kowa Research Institute, Pharmasset, Inc., Pfizer Inc., Janssen/Tibotec Therapeutics, Merck & Co., Tobira Therapeutics, ViiV Healthcare
- ❑ **Data Safety Monitoring Boards:**
  - Janssen/Tibotec Therapeutics and ViiV Healthcare

# Common Design Elements of Oral PrEP Trials

- **Community consultation**
  - To assess trial feasibility, acceptability and implementation
- **Random assignment to placebo or intervention groups receiving either TDF/FTC or TDF**
- **Daily dosing of study medication in oral arms of all studies**
- **Data and safety monitoring board**
  - Periodic expert panel reviews to ensure data quality and participant safety

# Common Design Elements of Oral PrEP Trials

- **Symptom assessment and laboratory tests for safety monitoring (e.g. liver enzymes and renal function)**
- **HIV testing, risk reduction and adherence counseling, adherence assessments at every visit**
- **Additional follow-up, viral resistance testing, and linkage to HIV care for participants who seroconvert during trial**
- **Efficacy determined by modified intention-to-treat (mITT)**
  - mITT - analysis based on the initial treatment assignment
  - Modified to exclude persons found to be acutely infected with HIV at the time of enrollment in the study

# Randomized, Controlled PrEP Efficacy Trials

Trial (Sponsor) Sample Size	Intervention vs. Placebo	Population	Location
<b>iPrEx</b> (NIH; Gates) <i>n=2499</i>	Oral TDF/FTC	MSM, transgender women	Peru, Ecuador, S Africa, Brazil, Thailand, US
<b>Partners PrEP</b> (Gates) <i>n=4747 couples</i>	Oral TDF/FTC Oral TDF	Heterosexual serodiscordant couples	Kenya, Uganda
<b>TDF2</b> (CDC) <i>n=1200</i>	Oral TDF/FTC	Sexually active adults	Botswana
<b>Bangkok Tenofovir</b> (CDC) <i>n=2413</i>	Oral TDF	Injection drug users	Thailand
<b>FEM-PrEP</b> (USAID, Gates, FHI 360) <i>n=1951</i>	Oral TDF/FTC	Heterosexual women	Kenya, S Africa, Tanzania
<b>VOICE</b> (MTN-003) <i>n=5029</i>	Oral TDF/FTC Oral TDF Vag 1% tenofovir gel	Heterosexual women	Uganda, S Africa, Zimbabwe

Grant et al. NEJM 2010; 363 :2587- 2599  
 Baeten et al NEJM 2012;367:399-410;CROI 2014: Abstract 43  
 Thigpen, et al. NEJM 2012;367:423-34

Choopanya et al. Lancet 2013 Jun 15;381(9883):2083-90  
 Van Damme, et al. NEJM. 2012;367:411-22  
 Marazzo et al. CROI 2013: Abstract 26LB

# Results of PrEP Efficacy Trials

## Detection of Tenofovir Levels in Blood Associated with Greater Efficacy

Study	Oral Regimen Dosed Daily	Relative Risk Reduction (95% CI)	
		All Subjects	Drug Detectable
iPrEx	TDF/FTC	0.44 (0.15 – 0.63)	<b>0.92</b> (0.40 – 0.99)



**Study drug:**  
**Enrollment:**  
**Sites:**

**Oral TDF/FTC**  
**2,499 MSM and transgender women**  
**Peru, Ecuador, South Africa,**  
**Brazil, Thailand, USA**

Table adapted from Hendrix, C. HIV Pre-Exposure Prophylaxis: Clinical Pharmacology Insights. CROI 2014, Oral Abstract 61  
TDF/FTC: tenofovir/emtricitabine  
MSM: Men who have sex with men

# Results of PrEP Efficacy Trials

## Detection of Tenofovir Levels in Blood Associated with Greater Efficacy

Study	Oral Regimen Dosed Daily	Relative Risk Reduction (95% CI)	
		All Subjects	Drug Detectable
iPrEX	TDF/FTC	0.44 (0.15 – 0.63)	<b>0.92</b> (0.40 – 0.99)
Partners PrEP	TDF	0.67 (0.44 – 0.81)	<b>0.86</b> (0.67 – 0.94)
	TDF/FTC	0.75 (0.55 – 0.87) <i>TDF vs TDF/FTC not significantly different</i>	<b>0.90</b> (0.58 - 0.98)



PARTNERS PrEP STUDY

**Study drug:**  
**Enrollment:**  
**Sites:**

**Oral TDF/FTC, Oral TDF**  
**4,747 heterosexual serodiscordant couples**  
**Kenya, Uganda**

Table adapted from Hendrix, C. HIV Pre-Exposure Prophylaxis: Clinical Pharmacology Insights. CROI 2014, Oral Abstract 61  
Baeten et al. CROI 2014: Abstract 43

# Results of PrEP Efficacy Trials

## Detection of Tenofovir Levels in Blood Associated with Greater Efficacy

Study	Oral Regimen Dosed Daily	Relative Risk Reduction (95% CI)	
		All Subjects	Drug Detectable
iPrEx	TDF/FTC	0.44 (0.15 – 0.63)	<b>0.92</b> (0.40 – 0.99)
Partners PrEP	TDF	0.67 (0.44 – 0.81)	<b>0.86</b> (0.67 – 0.94)
	TDF/FTC	0.75 (0.55 – 0.87) <i>TDF vs TDF/FTC not significantly different</i>	<b>0.90</b> (0.58 – 0.98)
Bangkok Tenofovir	TDF	0.49 (0.10 – 0.72)	<b>0.74</b> (0.17– 0.94)

### **Bangkok Tenofovir Study**

**Study drug:**

**Oral TDF**

**Enrollment:**

**2,413 Injection drug users**

**Sites:**

**Thailand**

Table adapted from Hendrix, C. HIV Pre-Exposure Prophylaxis: Clinical Pharmacology Insights. CROI 2014, Oral Abstract 61  
Baeten et al. CROI 2014: Abstract 43

# Results of PrEP Efficacy Trials

## Detection of Tenofovir Levels in Blood Associated with Greater Efficacy

Study	Oral Regimen Dosed Daily	Relative Risk Reduction (95% CI)	
		All Subjects	Drug Detectable
iPrEx	TDF/FTC	0.44 (0.15 - 0.63)	<b>0.92</b> (0.40 – 0.99)
Partners PrEP	TDF	0.67 (0.44 – 0.81)	<b>0.86</b> (0.67–0.94)
	TDF/FTC	0.75 (0.55 – 0.87)	<b>0.90</b> (0.58–0.98)
		<i>TDF vs TDF/FTC not significantly different</i>	
Bangkok Tenofovir	TDF	0.49 (0.10 – 0.72)	<b>0.74</b> (0.17–0.94)
			<b>% Pts with Detectable Drug</b>
TDF2	TDF/FTC	0.62 (0.22 – 0.83)	50% among HIV infected 80% among not infected

# TDF2

**Study drug:**  
**Enrollment:**  
**Sites:**

**Oral TDF/FTC**  
**1,200 sexually active adults**  
**Botswana**

Table adapted from Hendrix, C. HIV Pre-Exposure Prophylaxis: Clinical Pharmacology Insights. CROI 2014, Oral Abstract 61  
Baeten et al. CROI 2014: Abstract 43  
Hendrix C. Cell 2013;155: 515-518.

Study	Oral Regimen Dosed Daily	Relative Risk Reduction (95% CI)	
		All Subjects	Drug Detectible
FEM-PrEP	TDF/FTC	Stopped due to futility	< 40% among all participants
VOICE	TDF TDF/FTC	Stopped due to futility Showed no efficacy	< 30% among all participants

- Poor adherence, as measured by detectable drug levels, was a major factor in lack of efficacy in both studies
- Self reported adherence was very high and was not predictive of outcome except when patients said that they did not take drug
- In VOICE, no behavioral measures correctly predicted adherence as measured by drug concentration in the blood

**Futility: stopping clinical trial when interim results suggest that it is unlikely to achieve statistically significant differences between treatment arm and placebo/control arm**

Table adapted from Hendrix, C. HIV Pre-Exposure Prophylaxis: Clinical Pharmacology Insights. CROI 2014, Oral Abstract 61  
 Baeten et al. CROI 2014: Abstract 43  
 Hendrix C. Cell 2013;155: 515-518.  
 van der Straten, et al. CROI 2014: Abstract 44  
 Snapinn S, Chen Mg, Jiang Q et al. Pharm Stat. 2006 Oct-Dec;5(4):273-81.

# Safety of Tenofovir-based PrEP in Clinical Trials

- ❑ **No significant differences in serious adverse events, renal function markers or deaths among patients taking study drug compared to those taking placebo**
- ❑ **Adverse events more common on TDF or TDF/FTC than placebo in any study included**
  - Short-duration nausea, vomiting; dizziness
  - Back pain; decreased weight
  - Mild elevation in liver enzymes; mild neutropenia (more with TDF/FTC than TDF)
  - Small but statistically significant decreases in bone mineral density; no difference in atraumatic fractures
- ❑ **Among women who became pregnant, study drug was not associated with increased pregnancy complications**

# HIV Resistance and PrEP

- ❑ **Viral resistance occurs when mutations arise in genetic material of HIV that help it to survive in presence of an antiretroviral drug**
- ❑ **Resistance means that a drug no longer works optimally, or at all, to suppress HIV**
- ❑ **Resistance to one antiretroviral drug can result in cross-resistance to others that have never been taken**
- ❑ **Persons who acquire HIV while taking TDF/FTC, or who have HIV before taking TDF/FTC for PrEP, are at risk for viral resistance that may limit treatment options**

# HIV Resistance in PrEP Trial Participants

- ❑ **Among persons with undetected acute infections before starting medication, resistance mutations found in**
  - 8 of 30 persons randomized to TDF/FTC or TDF
- ❑ **Among persons infected after enrollment**
  - None randomized to TDF/FTC or TDF had TDF-resistant viruses (0 out of 263)
  - 5 had FTC-resistant viruses (1 in VOICE, 4 in FEM PrEP)
- ❑ **In IPrEx and Partners PrEP, among persons infected after enrollment**
  - 6 out of 99 randomized to TDF/FTC or TDF had low levels of minor resistance mutations, found using more sensitive research assays
  - Clinical implications unknown
- ❑ **Viral resistance risk is highest if starting PrEP when already HIV infected, especially those recently infected**
- ❑ **HIV testing before and during use is critical**

# No Evidence of Increased Risk Behavior Seen in Clinical Trials

Trial	Risk Behavior Assessed
<b>iPrEx</b>	<ul style="list-style-type: none"> <li>• Episodes of receptive anal sex declined</li> <li>• Condom use during receptive anal sex increased</li> <li>• No difference in condom use by perceived treatment group</li> </ul>
<b>US MSM Safety Study</b>	<ul style="list-style-type: none"> <li>• Number of partners and percent reporting anal sex without condom declined</li> <li>• Episodes of anal sex without condom remained stable</li> </ul>
<b>Partners PrEP</b>	<ul style="list-style-type: none"> <li>• HIV uninfected participants reported declines in sex without condom use</li> </ul>
<b>TDF2</b>	<ul style="list-style-type: none"> <li>• Reported number of sex partners declined</li> <li>• Percent reporting sex without condom remained stable</li> </ul>
<b>Bangkok Tenofovir</b>	<ul style="list-style-type: none"> <li>• Reports of injecting drugs, sharing needles, and sex with more than 1 partner in preceding 3 months declined</li> </ul>

# Implementation Insights from PrEP Trials

- ❑ **TDF-based PrEP can be highly effective in reducing HIV acquisition risk- up to 92% in these studies - *if* medication adherence is high**
- ❑ **Risk of viral resistance highest if beginning PrEP with unrecognized HIV infection**
  - Need to test for HIV infection, ideally both acute and established, before and during use
- ❑ **Risk of acquiring HIV is not completely eliminated:**
  - Combine PrEP with other prevention methods for optimal results
    - Consistent and correct condom use
    - Substance use treatment programs, use of injection equipment that has not been used by other persons
    - Antiretroviral treatment for HIV-infected partner in HIV-discordant couples

# Implementation Insight from PrEP Trials

- ❑ **Safety monitoring will be important in real-world setting**
- ❑ **Health care providers who are not HIV specialists need comprehensive education about PrEP**
  - How to talk with patients about benefits and risks of PrEP
  - How to initiate and monitor PrEP to minimize toxicity and maximize effectiveness
  - How to discuss and support adherence
  - How to support other risk reduction strategies
  - How to manage HIV infection if it occurs

# Program and Policy Challenges for Delivery of PrEP



**Dawn K. Smith, MD, MS, MPH**

*Biomedical Interventions Activity Lead*

Prevention with Negatives Team

Epidemiology Branch, Division of HIV/AIDS Prevention

NCHHSTP



U.S. Department of  
Health and Human Services  
Centers for Disease  
Control and Prevention

# FDA Approval and Plans for Mitigating Health Risks for PrEP Use

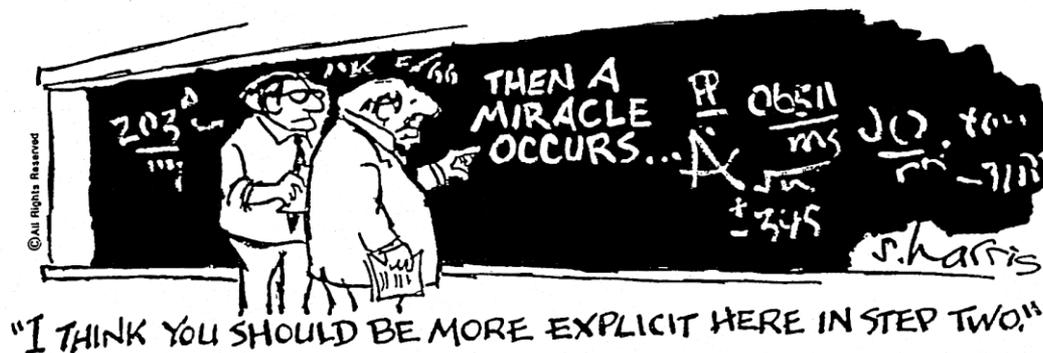
## □ July 2012 approval of Truvada®

- Indication for PrEP with sexually-active adults
- Risk Evaluation and Mitigation Strategy (REMS)
  - No restriction to specific providers or dispensing sites
  - Required medication guide and provider training
  - Required educational materials for HIV-negative persons
  - Annual assessment of effectiveness of REMS
- Elements to Assure Safe and Effective Use
  - Added language to package insert
    - Required HIV testing (boxed warning)
    - Indications/contraindications for prescribing PrEP
    - Strict adherence to daily dosing
    - Use in combination with other prevention methods

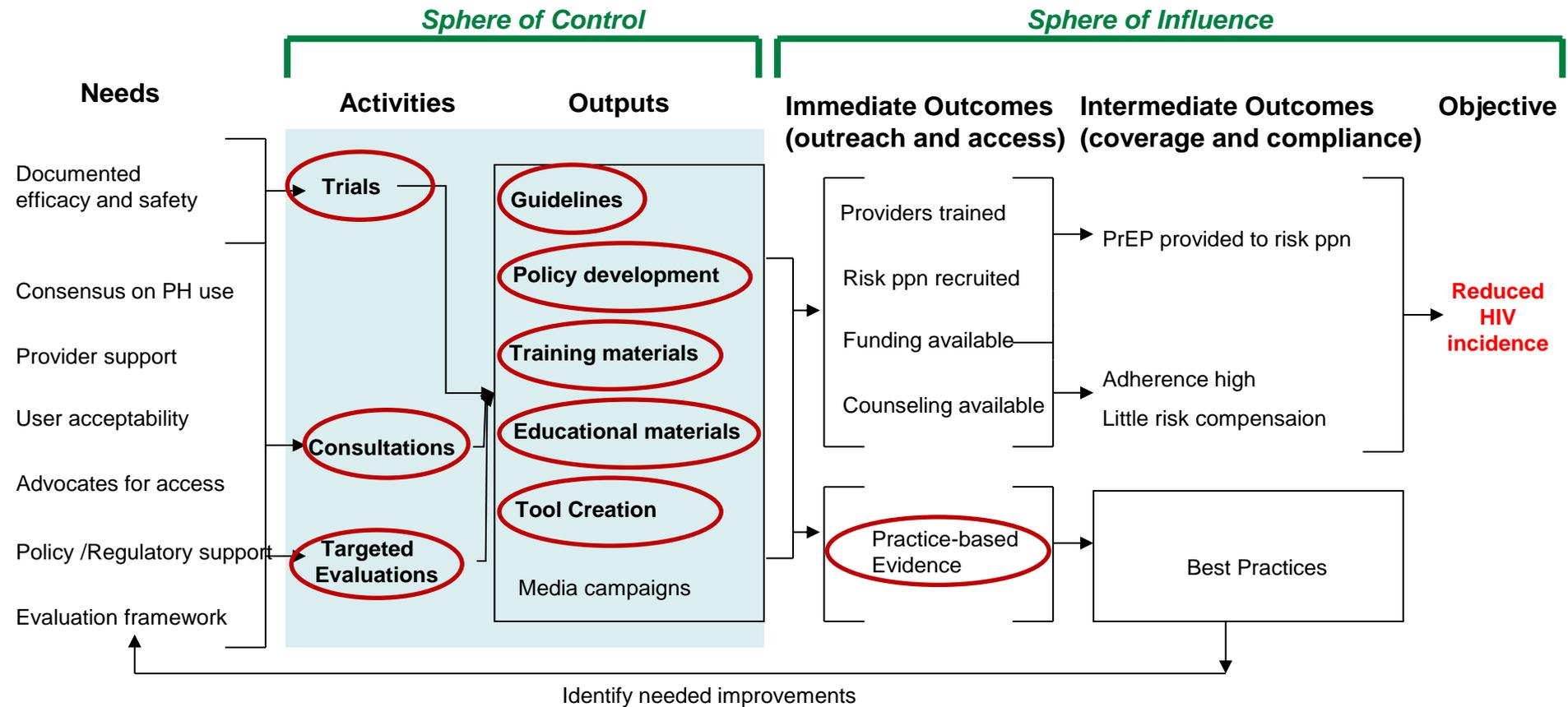
# Implementation in Context of Rapidly Evolving Evidence Base

## ❑ Need to understand how to support PrEP when delivered as clinical HIV prevention in communities

- Solicited lessons learned from implementation and evaluation science
- Learn what providers and potential users know about PrEP
  - Focus group with young adults in Atlanta
  - Questions added to an existing clinician survey (DocStyles)



# “Roadmap” for PrEP Implementation in the US



# External Stakeholder and Expert Engagement

## Guidelines Work Groups

- Clinical Care
- Clinic-based Counseling
- PrEP integration with other prevention services
- IDU
- MSM
- Heterosexual men
- Women
- Adolescents

## Technical Expert Meetings

- Public Health Ethics
- Monitoring and Evaluation
- Financing/Reimbursement
- HIV discordant couples and conception/pregnancy
- Network Science
- Public Health Law
- Insurers

# Supporting Introduction and Scale Up for Public Health Impact

- ❑ **Adapting interim guidance as the evidence evolved**
  - Men who have sex with men, 2011
  - Heterosexually active adults, 2012-2013
  - Injection drug users, 2013
  
- ❑ **Public Health Service Clinical Practice Guidelines for PrEP Use in the US (May 14, 2014)**
  - These Clinical Practice Guidelines replace the previous interim guidance documents

# Public Health Service Clinical Practice Guidelines: Key Messages

## ❑ **Daily, oral PrEP with Truvada®**

- Is recommended as one prevention option for persons at substantial risk of HIV infection including:
  - Sexually-active MSM
  - Heterosexually active men and women
  - Injection drug users
- Should be discussed with HIV discordant couples for use during conception and pregnancy
- Use should be weighed carefully for adolescent minors

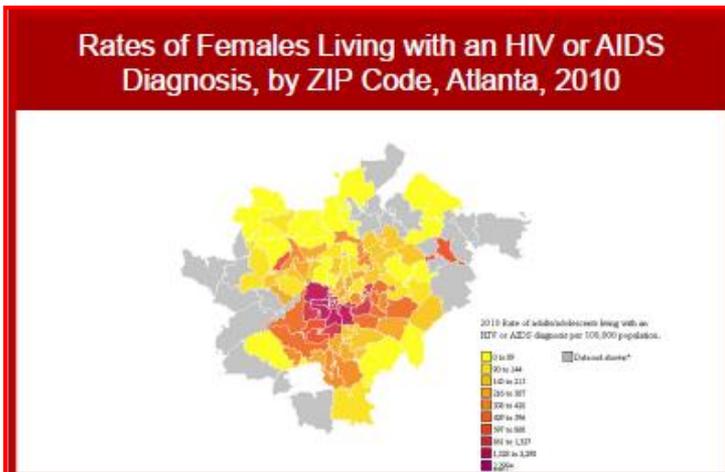
## ❑ **Support medication adherence and risk reduction practices**

# Indications for PrEP Use by Subpopulation

	Men Who Have Sex with Men	Heterosexual Women and Men	Injection Drug Users
Detecting substantial risk of acquiring HIV infection	<ul style="list-style-type: none"> <li>• HIV-positive sexual partner</li> <li>• Recent bacterial STI</li> <li>• High number of sex partners</li> <li>• History of inconsistent or no condom use</li> <li>• Commercial sex work</li> </ul>	<ul style="list-style-type: none"> <li>• HIV-positive sexual partner</li> <li>• Recent bacterial STI</li> <li>• High number of sex partners</li> <li>• History of inconsistent or no condom use</li> <li>• Commercial sex work</li> <li>• In high-prevalence area or network</li> </ul>	<ul style="list-style-type: none"> <li>• HIV-positive injecting partner</li> <li>• Sharing injection equipment</li> <li>• Recent drug treatment (but currently injecting)</li> </ul>

# Indications for PrEP Use by Subpopulation

	Men Who Have Sex with Men	Heterosexual Women and Men	Injection Drug Users
Detecting substantial risk of acquiring HIV infection	<ul style="list-style-type: none"> <li>• HIV-positive sexual partner</li> <li>• Recent bacterial STI</li> <li>• High number of sex partners</li> <li>• History of inconsistent or no condom use</li> <li>• Commercial sex work</li> </ul>	<ul style="list-style-type: none"> <li>• HIV-positive sexual partner</li> <li>• Recent bacterial STI</li> <li>• High number of sex partners</li> <li>• History of inconsistent or no condom use</li> <li>• Commercial sex work</li> <li>• In high-prevalence area or network</li> </ul>	<ul style="list-style-type: none"> <li>• HIV-positive injecting partner</li> <li>• Sharing injection equipment</li> <li>• Recent drug treatment (but currently injecting)</li> </ul>



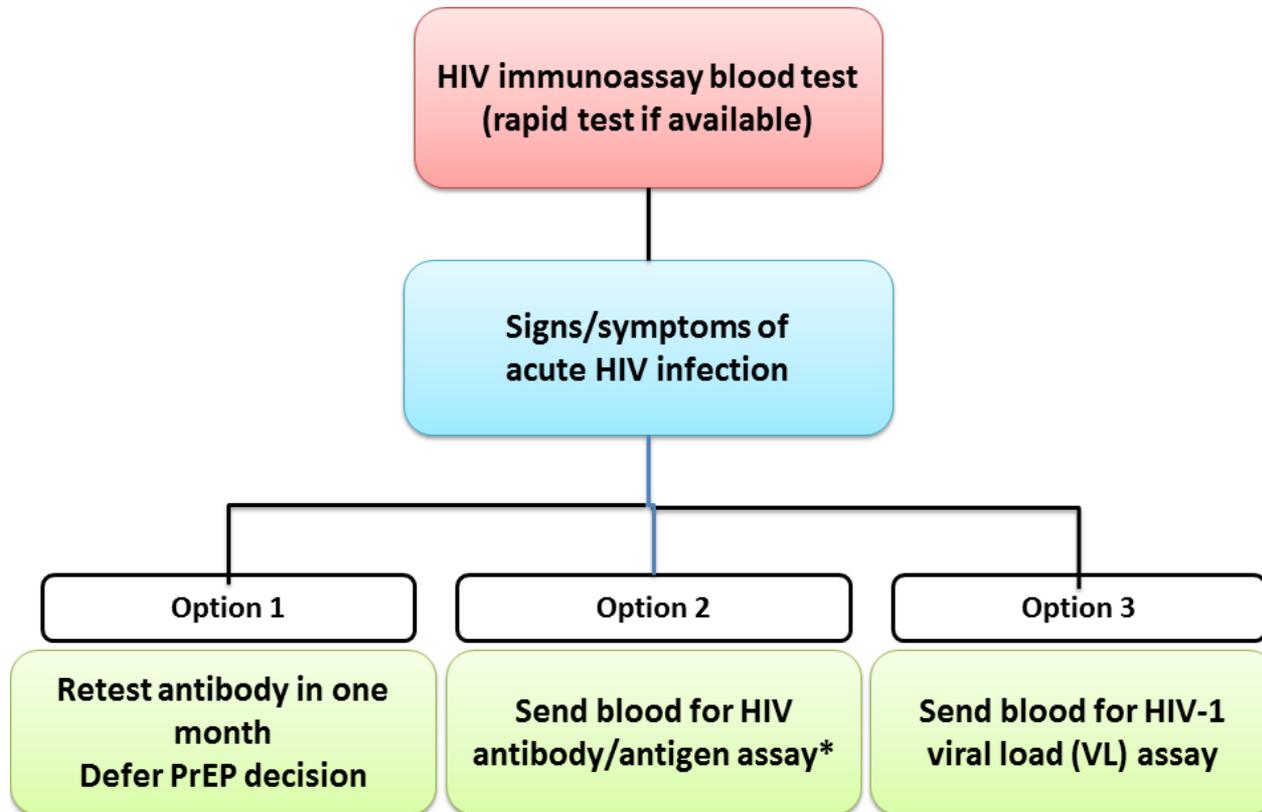
# Indications for PrEP Use by Subpopulation

	Men Who Have Sex with Men	Heterosexual Women and Men	Injection Drug Users
Detecting substantial risk of acquiring HIV infection	<ul style="list-style-type: none"> <li>• HIV-positive sexual partner</li> <li>• Recent bacterial STI</li> <li>• High number of sex partners</li> <li>• History of inconsistent or no condom use</li> <li>• Commercial sex work</li> </ul>	<ul style="list-style-type: none"> <li>• HIV-positive sexual partner</li> <li>• Recent bacterial STI</li> <li>• High number of sex partners</li> <li>• History of inconsistent or no condom use</li> <li>• Commercial sex work</li> <li>• In high-prevalence area or network</li> </ul>	<ul style="list-style-type: none"> <li>• HIV-positive injecting partner</li> <li>• Sharing injection equipment</li> <li>• Recent drug treatment (but currently injecting)</li> </ul>

# Assessing for Contraindications and Prescribing PrEP

	Men Who Have Sex with Men	Heterosexual Women and Men	Injection Drug Users
Clinically eligible	<ul style="list-style-type: none"> <li>• Documented negative HIV test result before prescribing PrEP</li> <li>• No signs/symptoms of acute HIV infection</li> <li>• Normal renal function; no contraindicated medications</li> <li>• Documented hepatitis B virus infection and vaccination status</li> </ul>		
Prescription	<ul style="list-style-type: none"> <li>• Daily, continuing, oral doses of TDF/FTC (Truvada®), ≤90-day supply</li> </ul>		

# Excluding Acute or Established HIV Infection



\* Use only HIV antigen/antibody tests that are approved by FDA for diagnostic purposes

# Follow-up Visits While Prescribing PrEP

	Men Who Have Sex with Men	Heterosexual Women and Men	Injection Drug Users
Other services	<p>Follow-up visits at least every 3 months to provide the following:</p> <ul style="list-style-type: none"> <li>• HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI symptom assessment</li> <li>• At 3 months and every 6 months thereafter, assess renal function</li> <li>• Every 6 months, test for bacterial STIs</li> </ul>		
	<ul style="list-style-type: none"> <li>• Do oral/rectal STI testing</li> </ul>	<ul style="list-style-type: none"> <li>• Assess pregnancy intent</li> <li>• Pregnancy test every 3 months</li> </ul>	<ul style="list-style-type: none"> <li>• Access to clean needles/syringes and drug treatment services</li> </ul>

# Follow-up Visits While Prescribing PrEP

	Men Who Have Sex with Men	Heterosexual Women and Men	Injection Drug Users
Other services	Follow-up visits at least every 3 months to provide the following: <ul style="list-style-type: none"> <li>HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI symptom assessment</li> <li>At 3 months and every 6 months thereafter, assess renal function</li> <li>Every 6 months, test for bacterial STIs</li> </ul>		
	<ul style="list-style-type: none"> <li>Do oral/rectal STI testing</li> </ul>	<ul style="list-style-type: none"> <li>Assess pregnancy intent</li> <li>Pregnancy test every 3 months</li> </ul>	<ul style="list-style-type: none"> <li>Access to clean needles/syringes and drug treatment services</li> </ul>

# Follow-up Visits While Prescribing PrEP

	Men Who Have Sex with Men	Heterosexual Women and Men	Injection Drug Users
Other services	Follow-up visits at least every 3 months to provide the following: <ul style="list-style-type: none"> <li>• HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI symptom assessment</li> <li>• At 3 months and every 6 months thereafter, assess renal function</li> <li>• Every 6 months, test for bacterial STIs</li> </ul>		
	<ul style="list-style-type: none"> <li>• Do oral/rectal STI testing</li> </ul>	<ul style="list-style-type: none"> <li>• Assess pregnancy intent</li> <li>• Pregnancy test every 3 months</li> </ul>	<ul style="list-style-type: none"> <li>• Access to clean needles/syringes and drug treatment services</li> </ul>

# Follow-up Visits While Prescribing PrEP

	Men Who Have Sex with Men	Heterosexual Women and Men	Injection Drug Users
Other services	Follow-up visits at least every 3 months to provide the following: <ul style="list-style-type: none"> <li>• HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI symptom assessment</li> <li>• At 3 months and every 6 months thereafter, assess renal function</li> <li>• Every 6 months, test for bacterial STIs</li> </ul>		
	<ul style="list-style-type: none"> <li>• Do oral/rectal STI testing</li> </ul>	<ul style="list-style-type: none"> <li>• Assess pregnancy intent</li> <li>• Pregnancy test every 3 months</li> </ul>	<ul style="list-style-type: none"> <li>• Access to clean needles/syringes and drug treatment services</li> </ul>

# Clinical Providers Supplement to Guidelines: Educational and Training Materials

## □ Patient factsheets

- PrEP
- Truvada®
- Acute HIV infection

## □ Provider materials

- Patient/Provider checklist
- Information on PrEP during conception, pregnancy, and breastfeeding
- HIV incidence risk index for MSM
- Potential PrEP practice quality measures
- Supplemental counseling information

# Tools for Implementation of PrEP in Clinical Practice

- ❑ Materials for persons considering PrEP
- ❑ Guide for billing codes
- ❑ Risk screening tools
  - Published for MSM
  - Under development for HIV-discordant couples, injection drug users

Choose an ARCH tool



## HOW TO TALK TO YOUR DOCTOR ABOUT PrEP

**Before Your Visit**

**Make an appointment** with your health care provider. Your doctor can help you to decide if PrEP would be a good choice for you.

**Do research.** Make a list of reasons that you think that PrEP would be a good choice for you.

**Think about your routine,** especially things that might make it easy or hard to take a daily medication.

**Make a health history list** for your doctor. That includes any past illnesses or concerns you have, as well as a list of your current medications (including supplements, herbs, etc.).

**Make sure a translator is available or bring someone who can translate** if you would prefer to speak a language other than English during your appointment.

**During Your Visit**

**Be clear.** Take out your notes and tell your doctor that you are interested in PrEP right away.

**Do not be shy.** Give your doctor all the details about your life that could be important to your health. Don't worry about being judged.

If your sex life is a hard topic to talk about, say that to your doctor. It will help to start the conversation.

**Ask questions.** You want to be sure that you understand what your doctor is telling you.

**Take notes** during your visit so that you can remember what your doctor said.

**After Your Visit**

**Review** your notes or any information provided by your doctor.

**Consider your options.** Your doctor gave you a lot of information. Now it is up to you to make the right decision for you.  
<http://www.cdc.gov/hiv/risk/behavior/index.html>

**Call your doctor** if you have more questions. Ask to speak to a nurse if your doctor is unavailable.

**Schedule tests** or follow-up appointments your doctor requested.

**Get your results** if you had tests done at your appointment.

**If you feel comfortable,** you may want to discuss this choice with your partners, family, or friends.

[www.cdc.gov/hiv/pdf/risk\\_PrEP\\_TalkingtoDr\\_FINALcleared.pdf](http://www.cdc.gov/hiv/pdf/risk_PrEP_TalkingtoDr_FINALcleared.pdf)

Smith DK, Pals SL, Herbst JH et al. J Acquir Immune Defic Syndr. 2012 Aug 1;60(4):421-7.

MSM: men who have sex with men

ARCH: Assessing the risk for contracting HIV

# Policy Development to Mitigate PrEP Costs

## ❑ Average retail pharmacy price for a one month supply of Truvada® is \$1400

- Negotiated drug price reductions
- Most private employer, school-based and public insurers (e.g. Medicaid) provide coverage for PrEP medications and care

## ❑ PrEP drug and co-pay assistance programs available

- Free medication for those with low income and no insurance coverage
  - Gilead Sciences
    - Free condoms and HIV testing can be provided
    - Free hepatitis B screening, and HIV resistance testing for those who seroconvert while on PrEP
  - Washington State

# Cost-effectiveness of PrEP

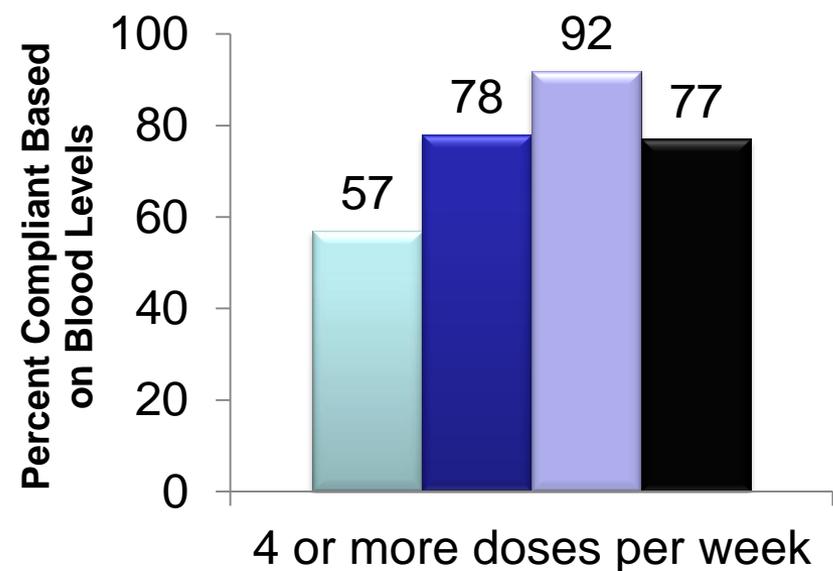
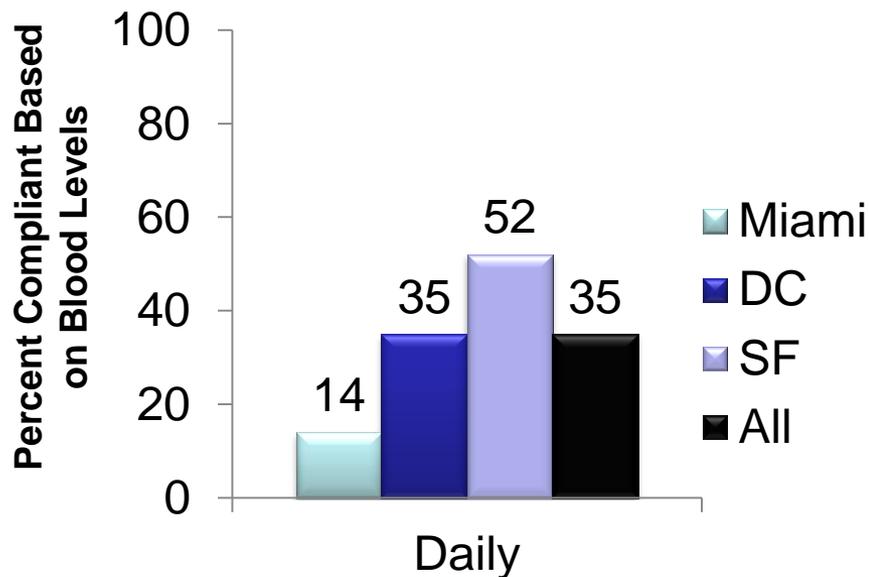
- ❑ **4 cost-effectiveness studies in MSM in the US**
- ❑ **Delivery of PrEP is most cost-effective when:**
  - **Targeted to populations with high HIV incidence**
  - **High coverage is achieved in targeted populations**
  - **Medication adherence is high**
  - **Cost of medication and clinical services are minimized**

# Estimating Early PrEP Uptake Using US Retail Pharmacy Claims Data

- ❑ **Analysis of a commercial pharmacy database**
  - Includes 55% of U.S. prescriptions
- ❑ **PrEP prescribers in ~700 US cities, 49 states**
  - 31% family practice and internal medicine
  - 17% non-physician prescribers (NP and PA)
  - 14% emergency medicine
  - 12% infectious disease
- ❑ **Prescriptions rose 8.5-fold**
  - 150 in 2011 to 1274 in 2012
  - 48% of prescribing for women
  - 14% for persons under age 25 years

# An Early Study to Evaluate PrEP Uptake and Adherence

- ❑ MSM recruited in STD clinics; 60% of eligible patients enrolled
- ❑ Medication adherence assessed at 4 weeks by blood drug level
  - Daily adherence suboptimal;  $\geq 4$  doses/week adherence higher
- ❑ Other modeled data\* suggest high efficacy may be achieved at  $\geq 4$  doses/wk



# Study of PrEP as Implemented in Community Health Centers



## ❑ Health Services Observational Cohort (SHIPP Study)

- Collects de-identified data from medical records
- Evaluate prescribing practices, patient outcomes, and service costs for all clinic patients receiving PrEP

## ❑ Medication Adherence Substudy (SHIPP Study)

- Offers participation with informed consent
- Collects dried blood spots to measure drug levels
- Provides adherence aids to those with suboptimal adherence

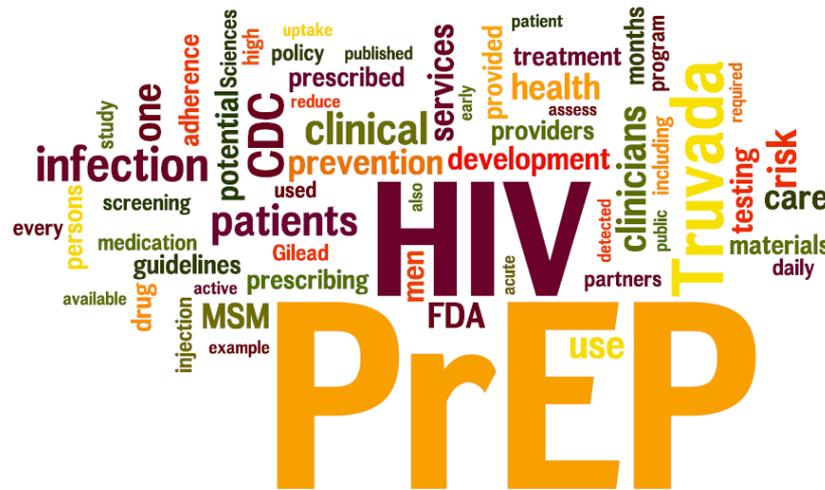
## ❑ Community Surveys (Context Matters Study)

- Clinician attitudes about PrEP and its provision in each clinic
- Knowledge and attitudes about PrEP among lay persons and key stakeholders in communities served by each clinic

# Role of PrEP in HIV Prevention

The United States will become a place where new HIV infections are rare...

*-National HIV/AIDS Strategy Vision Statement*



# Clinician Resources

Public Health Service Guidelines	<a href="http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf">www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf</a>
Providers' Supplement	<a href="http://www.cdc.gov/hiv/pdf/guidelines/PrEPProviderSupplement2014.pdf">www.cdc.gov/hiv/pdf/guidelines/PrEPProviderSupplement2014.pdf</a>
REMS clinician materials	<a href="http://www.truvadapreprems.com/truvadaprep-resources">www.truvadapreprems.com/truvadaprep-resources</a>
Medication Assistance Programs	<a href="http://www.nastad.org/docs/PrEP%20and%20PEP%20PAP%20fact%20sheet.pdf">www.nastad.org/docs/PrEP%20and%20PEP%20PAP%20fact%20sheet.pdf</a>
Co-Pay Assistance Program	<a href="http://www.gileadcopay.com/">www.gileadcopay.com/</a>
Free condoms for patients	<a href="https://start.truvada.com/individual/truvadaprep-patient-resources">https://start.truvada.com/individual/truvadaprep-patient-resources</a>
Free HIV testing for patients	<a href="https://start.truvada.com/hcp#">https://start.truvada.com/hcp#</a>
Adolescent Law Analysis	<a href="http://www.sciencedirect.com/science/article/pii/S0749379712007118">www.sciencedirect.com/science/article/pii/S0749379712007118</a>
<u>Online HIV Data maps:</u> CDC NCHHSTP Atlas	<a href="http://www.cdc.gov/nchhstp/atlas">www.cdc.gov/nchhstp/atlas</a>
AIDSVu	<a href="http://aidsvu.org/">aidsvu.org/</a>