HIV Pre-Exposure Prophylaxis (PrEP): Challenges and Opportunities

Josh Havens, PharmD
Clinical Pharmacist, UNMC HIV Program

Sara Hurtado Bares, MD
Assistant Professor, Division of Infectious Diseases

University of Nebraska Medical Center

Nebraska Medicine

Disclosures

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Objectives

1. Provide brief overview of PrEP
2. Describe some common challenges with PrEP management and implementation
3. Describe opportunities for PrEP access and scale-up

Introductions

Familiar with PrEP before today's talk?

Referred patients for PrEP?

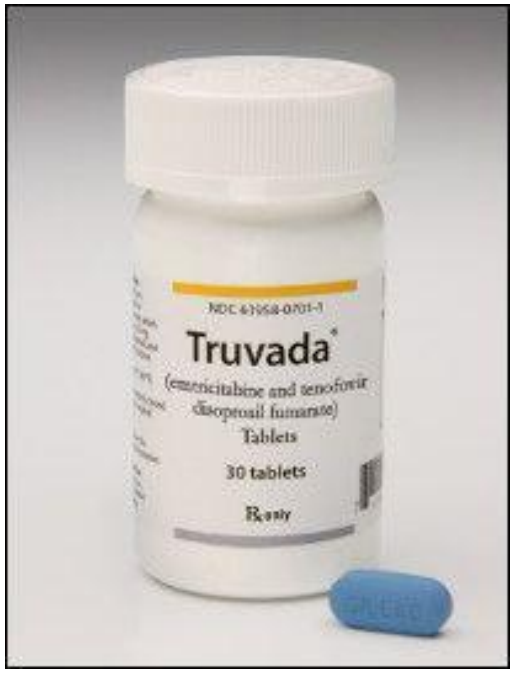
Prescribed PrEP?

What is PrEP?

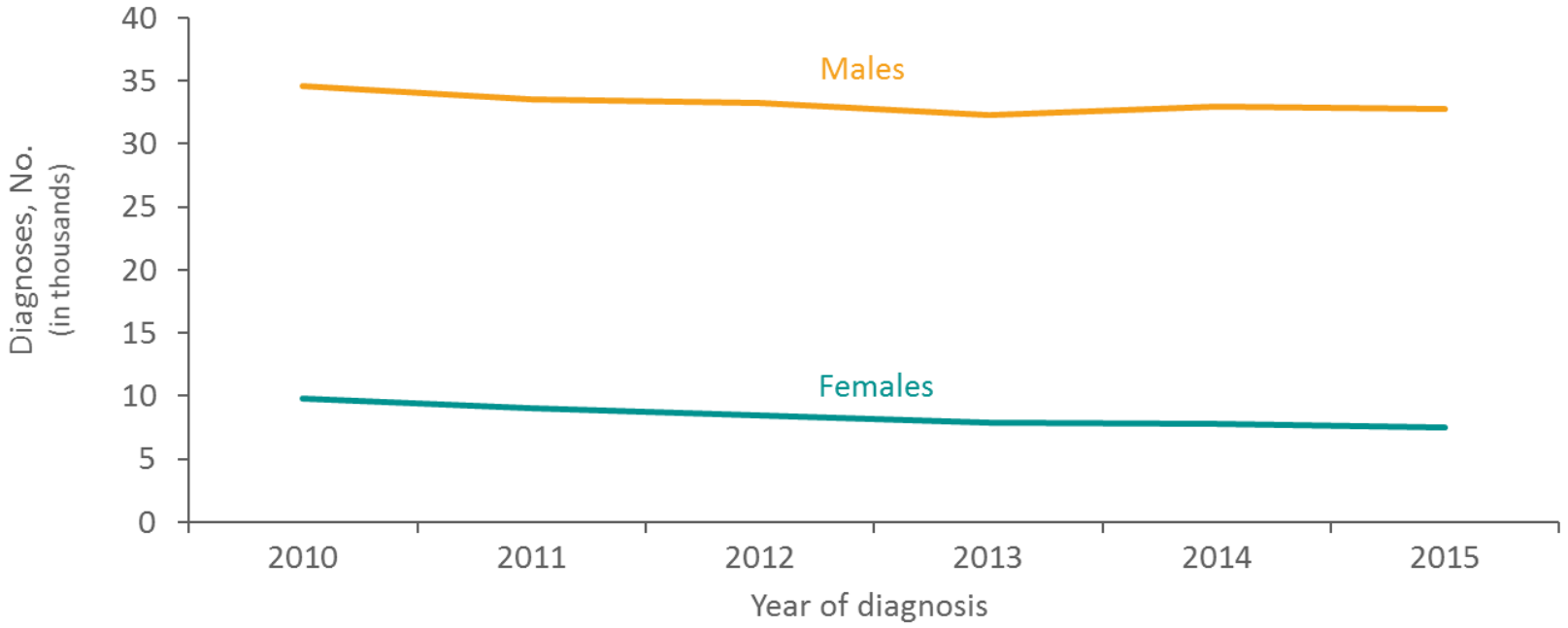
PrEP (pre-exposure prophylaxis)

- Strategy of administering antiretrovirals to HIV-uninfected, at-risk individuals in order to *prevent* HIV infection
- Similar strategies: malaria prophylaxis, oral contraceptives

Tenofovir-emtricitabine (TDF/FTC or Truvada) was approved for HIV PrEP by the FDA in July 2012



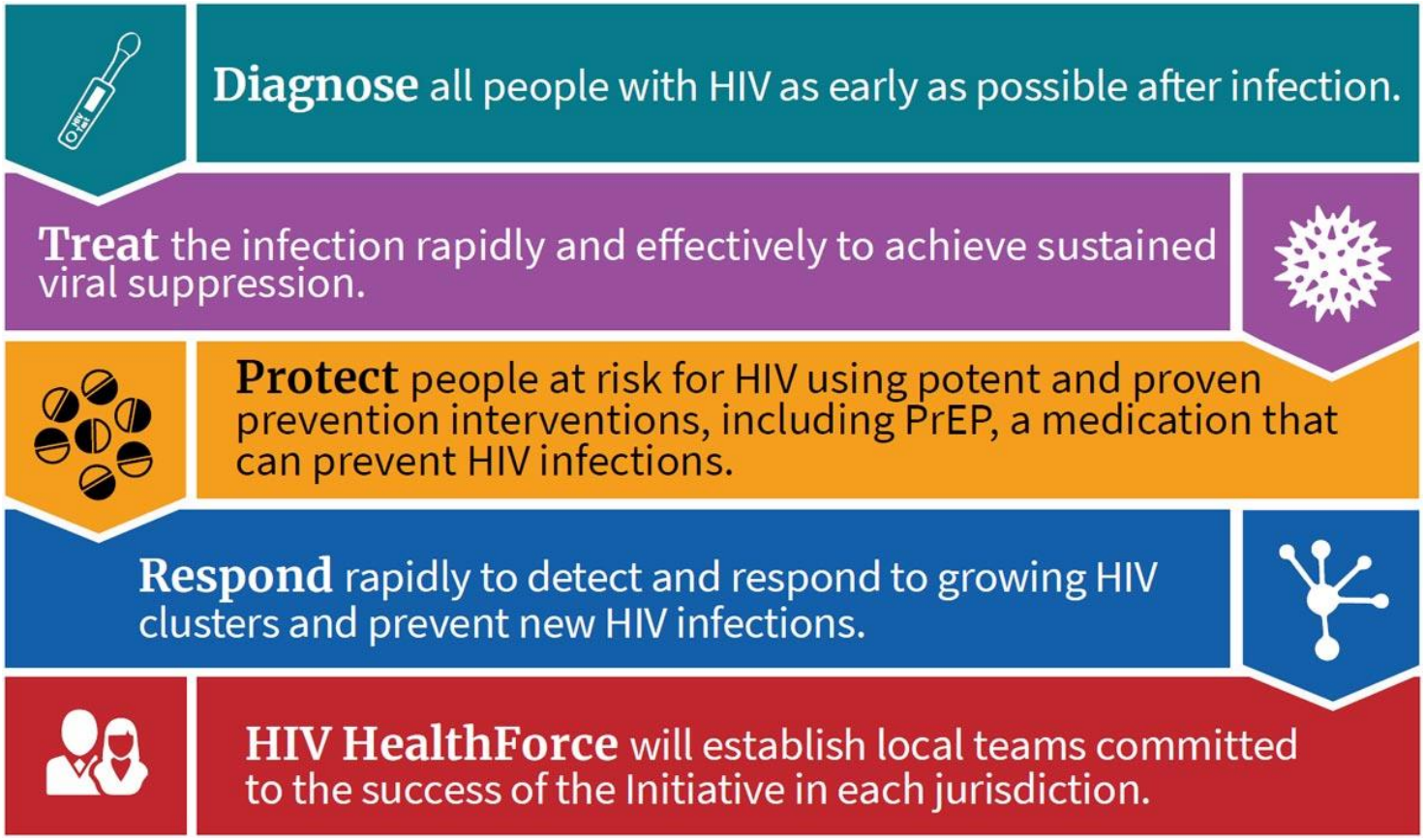
Why do we need PrEP?



https://www.cdc.gov/hiv/library/slideSets/index.html

Why do we need PrEP?

Ending the HIV Epidemic: A Plan for America



Why do we need PrEP?

An HIV provider's perspective…

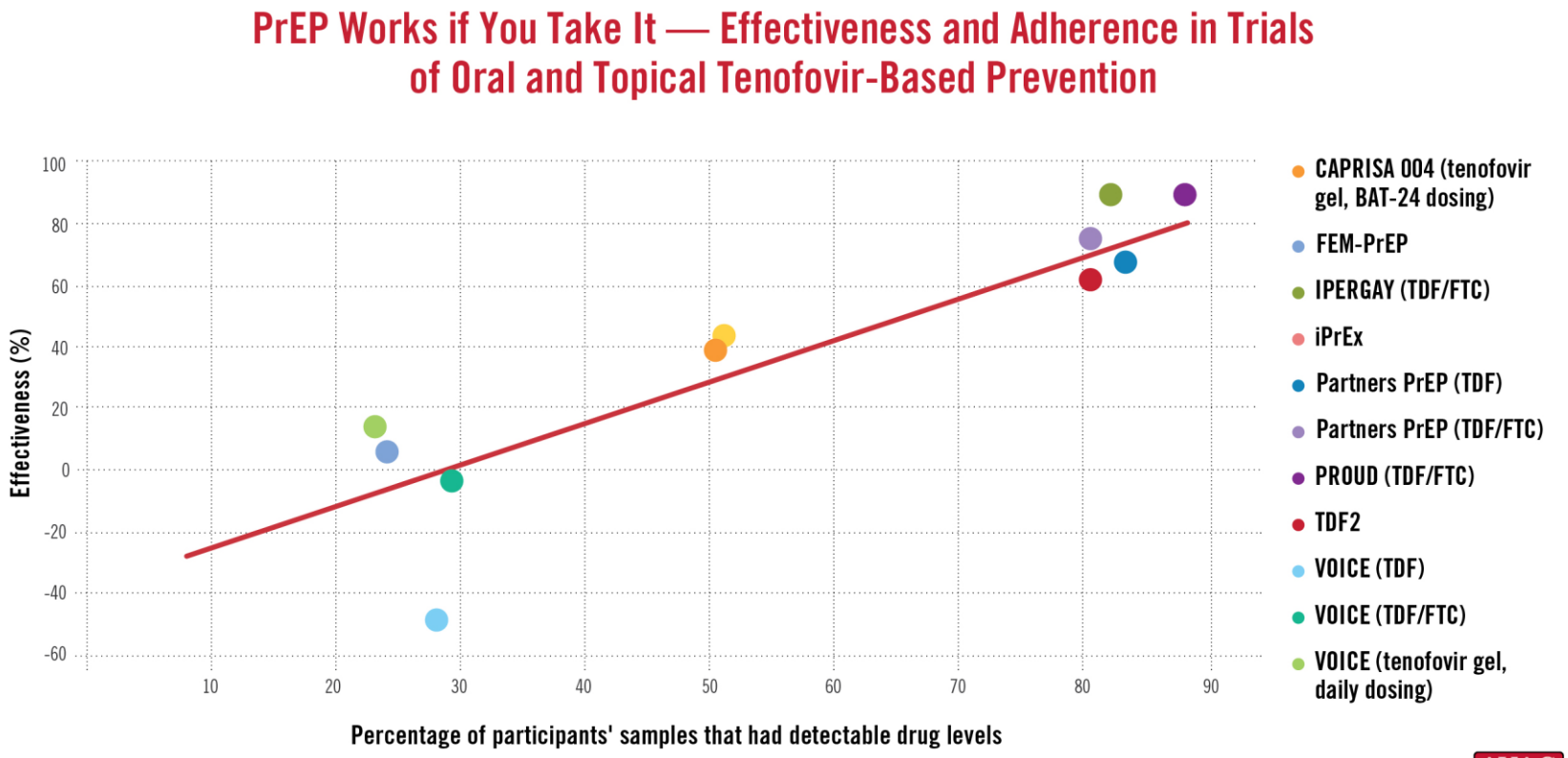
How effective is PrEP?

PrEP Trials

Study	Risk Category	Intervention	Efficacy
VOICE	Heterosexual Women	TDF	-49%
		FTC/TDF	-4%
FEM-PrEP		FTC/TDF	6%
Partners PrEP		TDF	71%
		FTC/TDF	66%
	Heterosexual Men	TDF	63%
		FTC/TDF	84%
IPrEx	MSM/TGW	FTC/TDF	44% (**92%**)
IPERGAY	MSM/TGW	FTC/TDF	86% (On Demand)
Bangkok Tenofovir Study	IVDU	TDF	49%

Grant RM, et al. *N Engl J Med*, 2010; Choopanya K, et al. *Lancet*, 2010; VanDamme L, et al. *N Engl J Med*, 2012; Baeten JM, et al. *Lancet ID*, 2014; Marrazzo JM et al. *N Engl J Med*, 2015; Molina JM, et al. *N Engl J Med*, 2015.

Adherence



AVAC
February 2016

Modified AVAC, https://www.avac.org/sites/default/files/infographics/PrEPbtn_EffectADHEREtrials.pdf

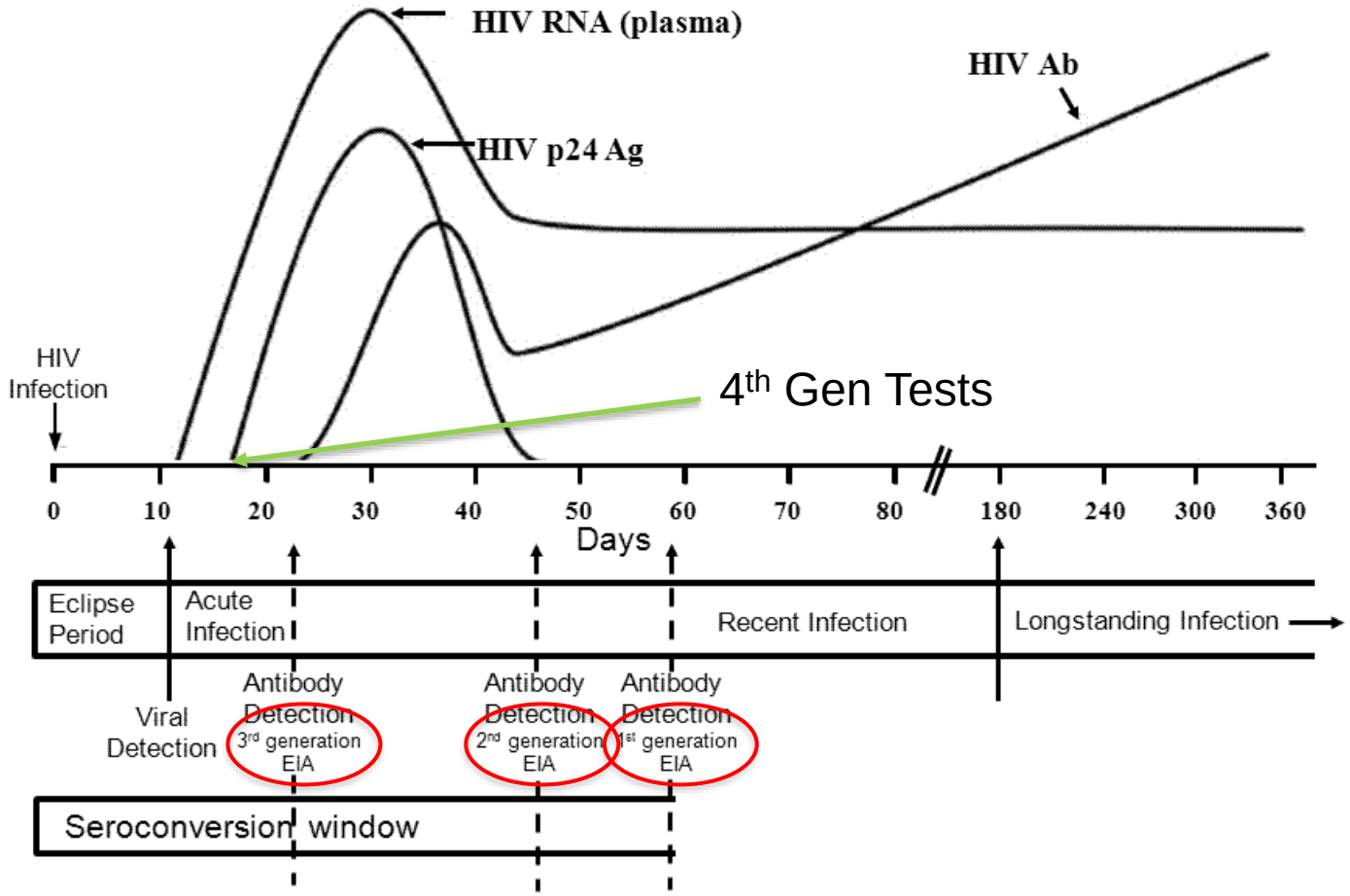
Who Should be Considered for PrEP?

1. IV Drug Use (IVDU)
2. Condomless sex
3. Multiple partners
4. History of STI
5. Previous need for HIV post-exposure prophylaxis
6. Illicit drug use (party drugs)
7. Commercial sex work
8. Sex with known HIV infected partner(s)?

PrEP Management

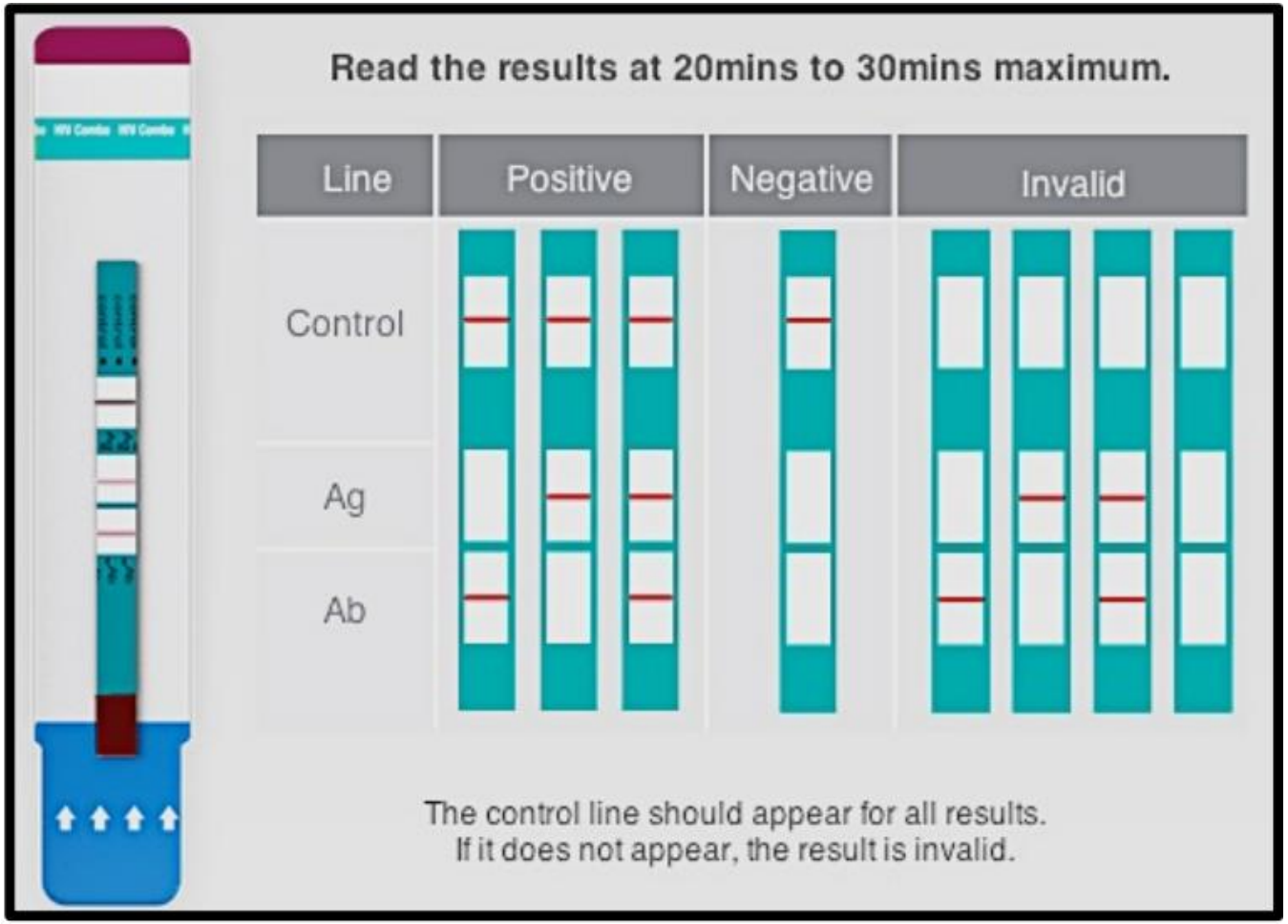
Clinical Measure	Frequency
HIV 1/2 antigen/antibody	Every 3 months
Basic Metabolic Panel	Baseline, 3 months, then every 6 months
HBV s antigen/s antibody	Baseline
HCV antibody	Baseline, then yearly in IVDU/MSM
Syphilis antibody	Baseline, then every 6 months
Chlamydia/Gonorrhea (all exposed sites)	Baseline, then every 3-6 months
Urine, pregnancy	Every 3 months

POC HIV Testing



Abstracted from: Government of Canada Public Health Agency of Canada, HIV Services

Alere Determine



Abstracted from: https://www.alere.com/en/home/product-details/determine-1-2-ag-ab-combo.html

PrEP Cost

Truvada® (emtricitabine/tenofovir DF) = ~$2,350 (WAC)

Lab	Frequency	Cost	PrEP Annual Cost
POC HIV Test	Baseline & Q3 Months	$25	$100
Metabolic Panel	Baseline, 3 Months, Q6 Months	$200	$600
HBV s antigen	Baseline	$125	$125
HBV s antibody	Baseline	$125	$125
HCV antibody	Baseline, Annually (IDU, MSM)	$125	$125
Syphilis antibody	Baseline, Q6 Months	$75	$150
Chlamydia/ Gonorrhea	Baseline, Q3-6 Months	$300 /site	$2,700
Total Annual PrEP Lab Cost (Gross)			$3,925

PrEP Cost

Total Annual PrEP Costs (Gross)		
Annual Lab Costs	$3,925	
Annual Drug Costs	~~$28,200~~ →	$0
Annual PrEP Costs	~~$32,125~~ →	$3,925

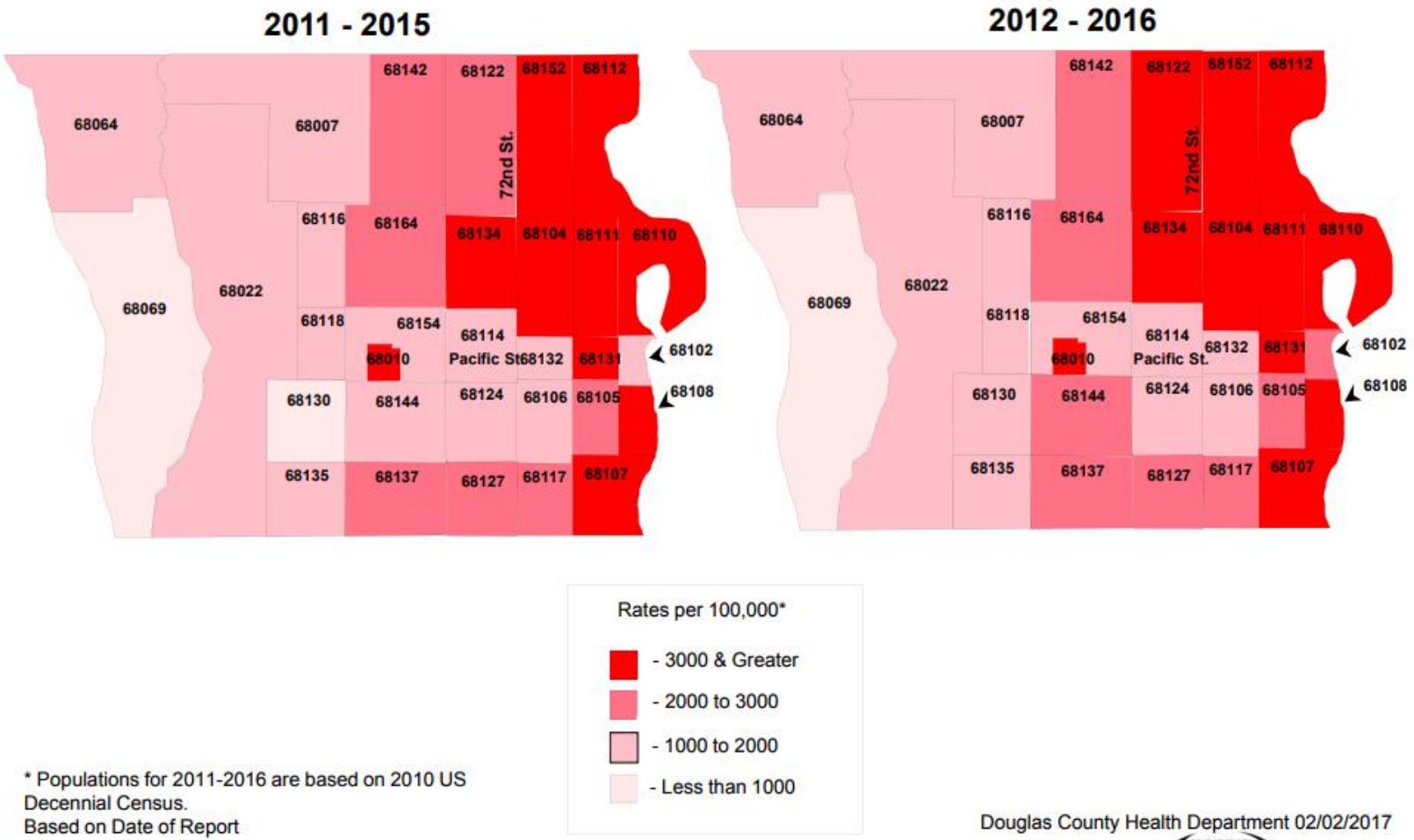
- There should rarely be a cost for FTC/TDF
  - High deductible plans
    - Copay cards
    - PAF, PANF grants
- Lab follow-up is always the cost factor
  - Sliding scale fee
  - Patient assistance

Nebraska HIV Disparities

	% of Total Population	% Living w/HIV	% New HIV Diagnosis (2016)
All Races	100%	100%	100%
White	85.4%	52%	50%
African American	**4%**	**28%**	**19%**
Hispanic	**7.2%**	**14.9%**	**20%**
Asian	1.8%	2%	4%
American Indian	0.7%	1.6%	4%
Other	0.1%	1.4%	0%
Multiracial	0.9%	0.1%	3%

Adapted from Nebraska DHHS HIV Surveillance Report, 2016

Chlamydia Rates by ZIP Code
Both Sexes, 15 to 24 Age Group
Douglas County, Nebraska - Five Year Average

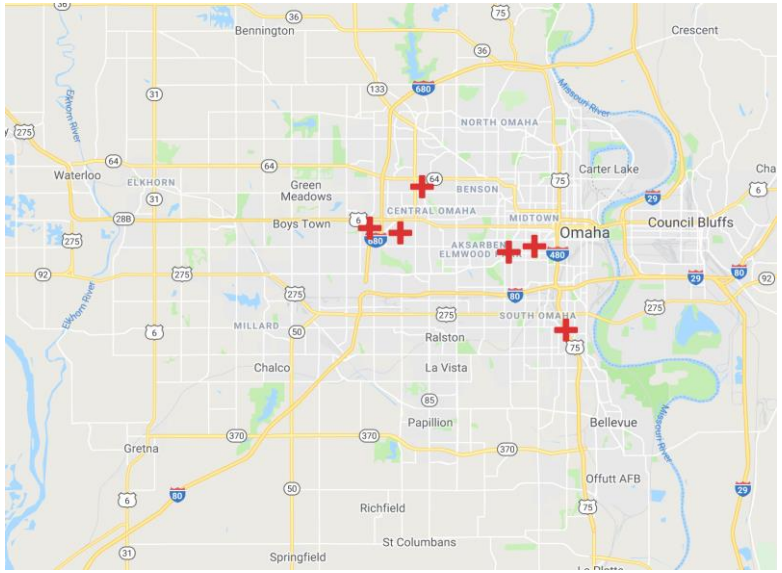


* Populations for 2011-2016 are based on 2010 US Decennial Census.
Based on Date of Report

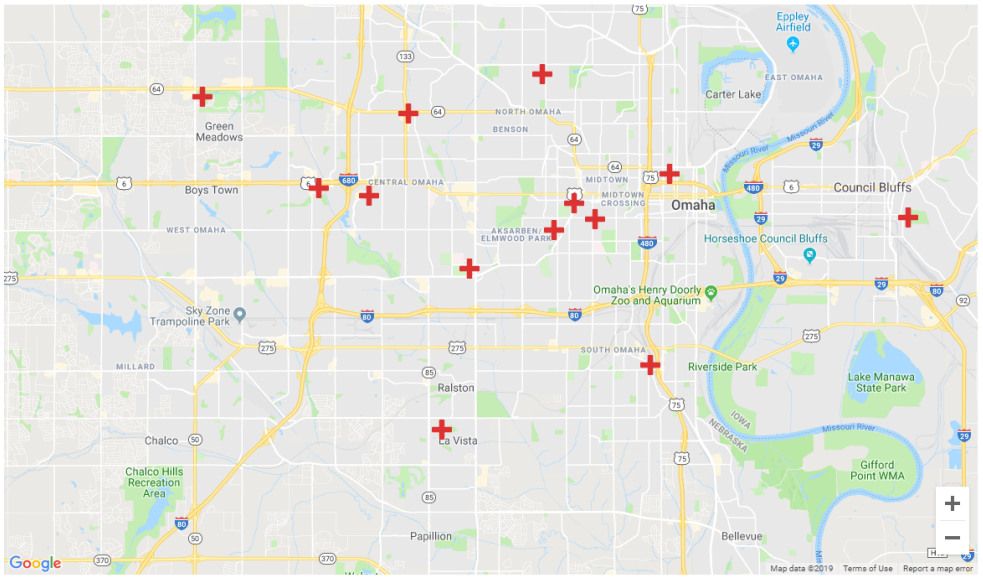
Douglas County Health Department 02/02/2017

PrEP Providers

Omaha (pop. ~500,000)



October 2018

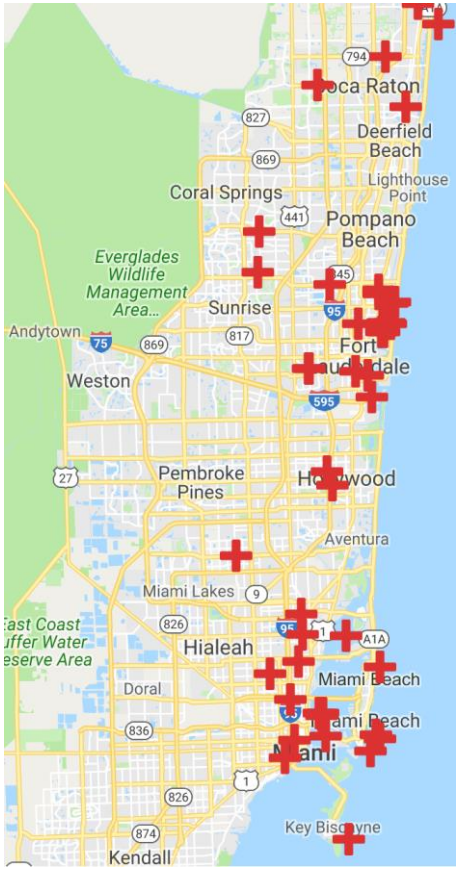


May 2019

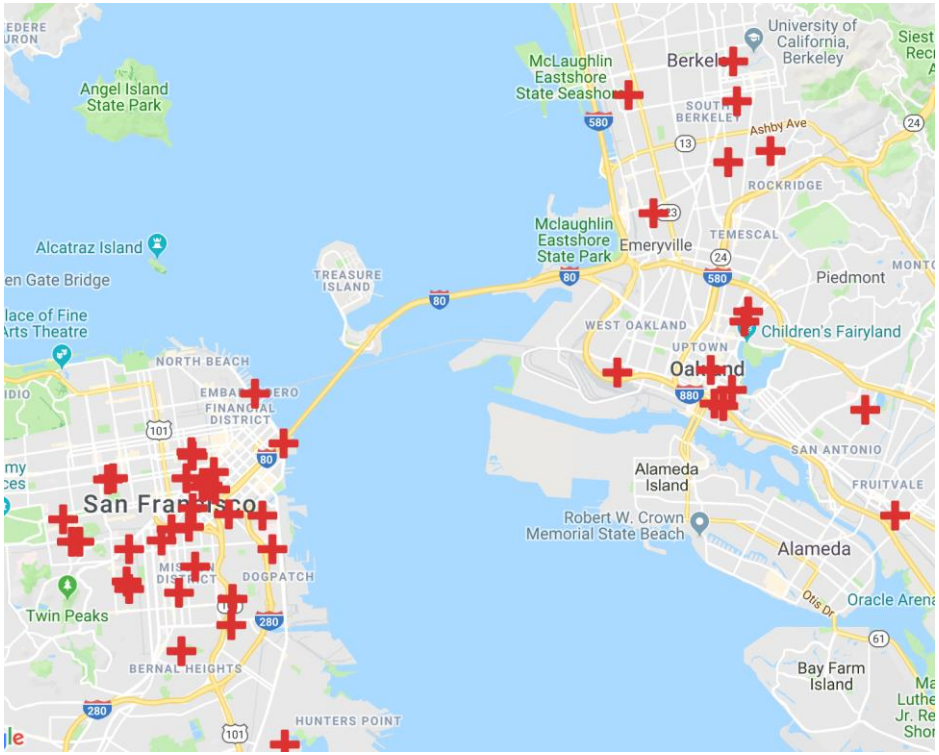
Preplocator.org

PrEP Providers

Miami (pop. ~500,000)

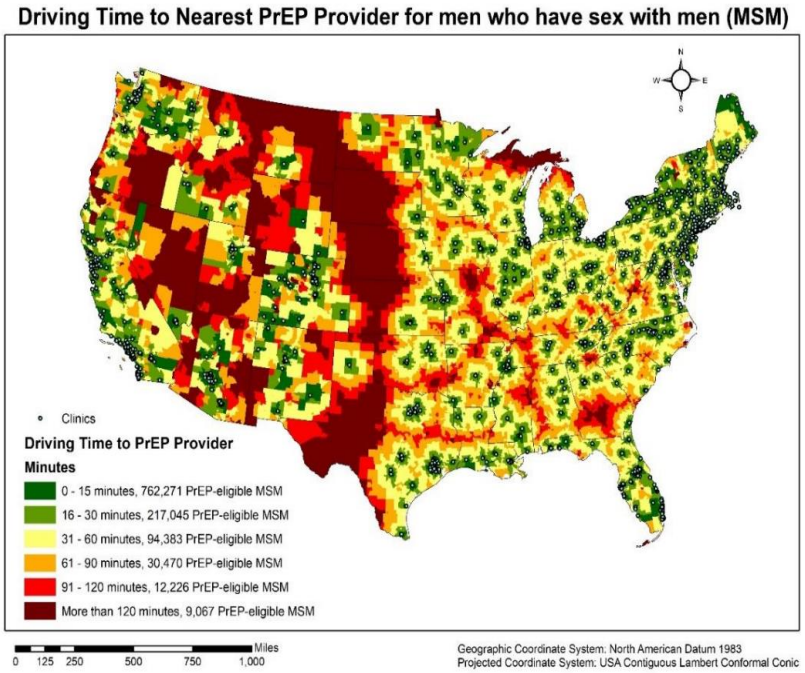


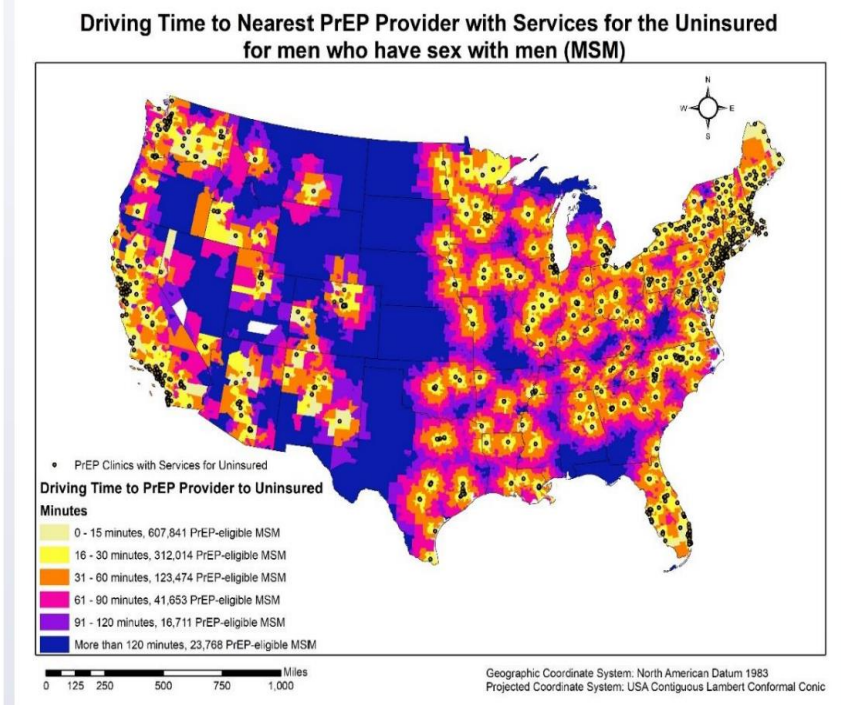
Oakland (pop. ~500,000)



Preplocator.org

PrEP Travel

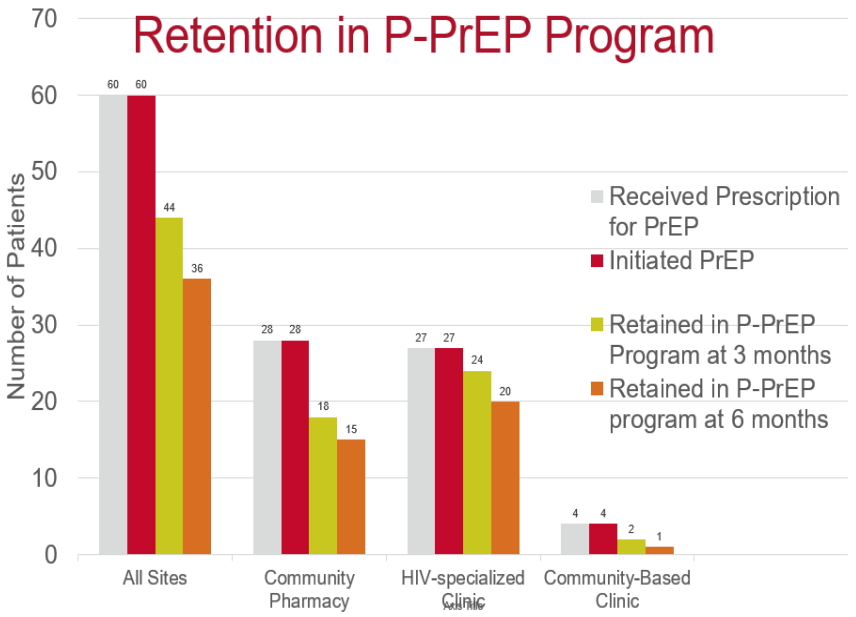




Weiss K, et al. CROI, 2018.

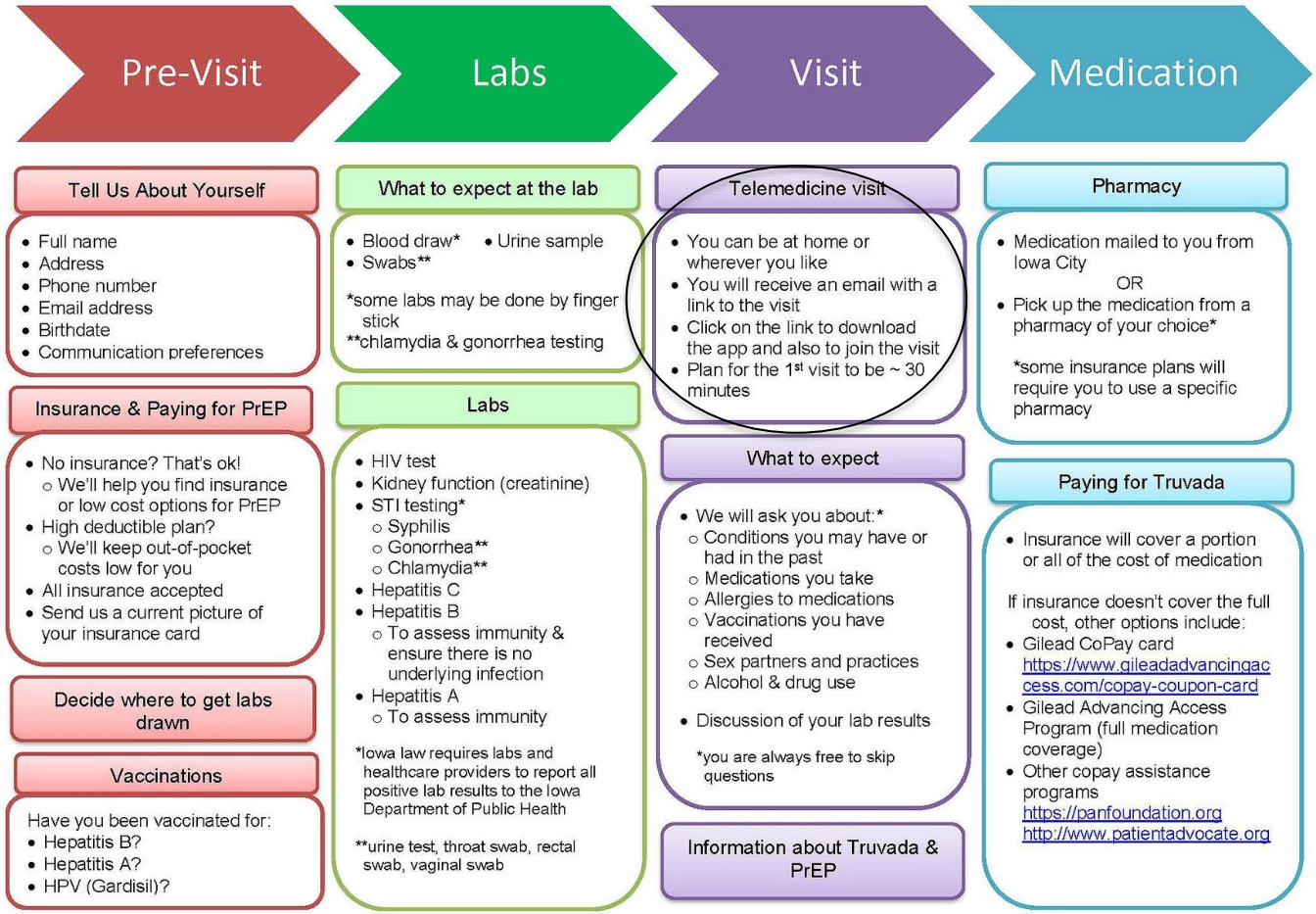
Pharmacist-Led PrEP

Demographics	Mean (Range or N %)
Age (years)	34 (20-61)
Male	57 (95%)
Race/Ethnicity	
White/Caucasian	50 (83%)
Black or African American	5 (8%)
Hispanic or Latino/a	5 (8%)
Other	3 (5%)
Insurance	
Private	48 (80%)
Medicare	1 (1.7%)
Uninsured	11 (18.3%)
HIV Risk Factor at Screening	
MSM	53 (88%)
Partner with HIV	17 (28%)
Transgender and High-Risk Sex	2 (3%)
Transactional Sex	1 (2%)
Stimulants and High-Risk Sex	1 (2%)
Anogenital STI in Last Year	19 (32%)



Bares S, et al. IDWeek 2018

Telehealth PrEP



https://www.prepiowa.org/what-to-expect

PrEP concerns

- Is it safe?
- Will it lead to resistance?
- Will it lead to riskier behavior?

Is PrEP Safe?

Start-up syndrome

- Nausea, vomiting, +/- dizziness occurred in <10% and primarily during first month

Renal safety

- 0.2% grade 2-4 elevations in creatinine among 5469 participants randomized to TDF/FTC

Bone safety

- ~1% loss of BMD
- Return to baseline with withdrawal
- Not associated with increased fracture risk

Grant RM, et al. NEJM 2010.
Baeten JM, et al. NEJM 2012.
Thigpen M, et al. NEJM 2012.
Van Damme L, et al. NEJM 2012.
Marrrazzo JM et al. NEJM 2015.
Solomon MM et al. AIDS 2014.
Liu AY et al. PLos One 2011.
Kasonde M et al. PloS One 2014.

Resistance

- Resistance rare in clinical trials of PrEP
- Analysis of drug resistance mutations among participants who acquired HIV in IPERGAY trial found that NONE of the participants had resistance mutations to TDF or FTC
- Most people who acquired HIV were probably not taking their PrEP and, when individuals don't take the antiretroviral they also don't develop resistance

Delaugerre C eta al. AIDS 2018 Aug 8.

Risk Compensation

Notion that PrEP use will lead to increase in high risk sexual activity due to perceived protection from PrEP

Concerns not unfounded

- PrEP does not protect against non-HIV STIs
- 42% of patients initiating PrEP in Kaiser health care system were diagnosed with STI during first year of use
- High STI rates may be attributable to increased screening or may reflect higher rates of condomless sex

BUT…

- Risk compensation hasn't led to higher rates of HIV acquisition
- Routine follow-up enables prompt detection and treatment of STIs
- Modeling study suggests STI testing and treatment as part of PrEP care will reduce bacterial STIs

https://www.cdc.gov/nchhstp/newsroom/2017/croi-prep-study.html

Case 1

DY, 28 y/o trans-female, presents for initial primary care establishment. She is in a relationship with an HIV infected man who is "undetectable."

How would you counsel DY on her HIV risk?

1. Condoms are needed to fully protect DY from HIV infection
2. Condoms are only needed when DY is on "bottom"
3. No condoms are needed with any sexual activity
4. PrEP and condoms are needed to prevent HIV

TaSP – Treatment as Prevention

Sexual Transmission

- HPTN 052: 1763 heterosexual discordant couples
- Partner: 900 serodiscordant couples, no condoms
- Partner2: 77K sexual events in MSM serodiscordant couples

Zero Transmissions

Case 2

Jim, 52 y/o, MSM, on Truvada for PrEP for 1 year presents for f/u. Reports 5 partners in past 3 months w/ intermittent condom use. No STI or acute viral syndrome s/s.

Lab	Result
POC HIV 1/2 Ag/Ab Test	Non-reactive
HBV serology	Immune
HCV Antibody	Non-reactive
CMP	Creatinine 1.49; CrCl 58 mL/min
STI screenings	Positive Rectal Chlamydia

	Today	3 mo ago	6 mo ago	9 mo ago	1 yr ago
Creatinine	1.49	1.34	1.26	1.15	1.28

Case 2

Jim, 52 yo, MSM, on PrEP with rising creatinine (creatinine clearance of 58 mL/min)

How would you manage this case?

1. Take off PrEP
2. Take PrEP less often
3. Work up renal dysfunction
4. Refer to ID
5. Change to different medicine

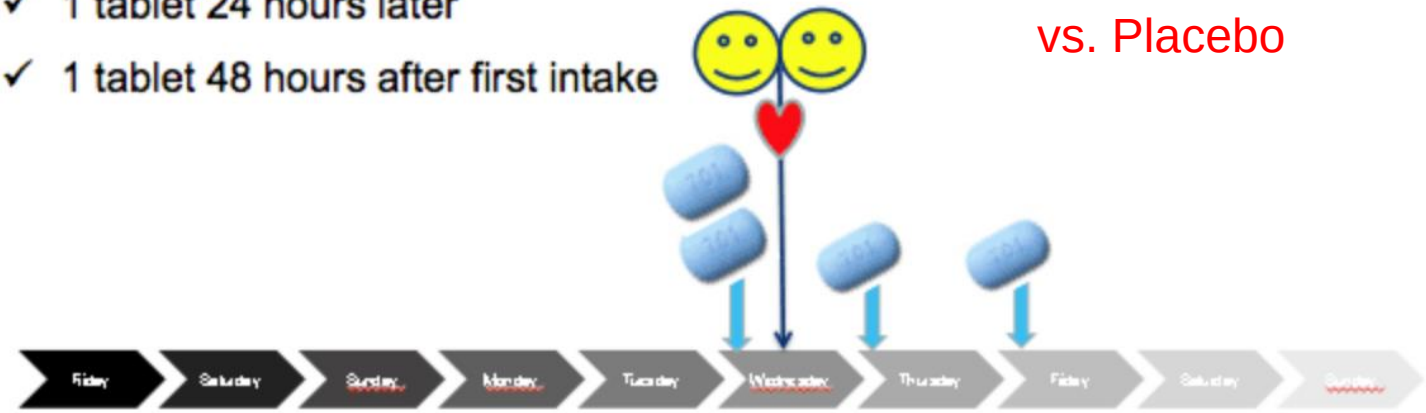
On-Demand PrEP

ipergay
ANRS
Intervention Préventive de l'Exposition aux Risques avec et pour les Gays

IPERGAY : Sex-Driven iPrEP

- ✓ 2 tablets 2-24 hours before sex
- ✓ 1 tablet 24 hours later
- ✓ 1 tablet 48 hours after first intake

86% Efficacious vs. Placebo

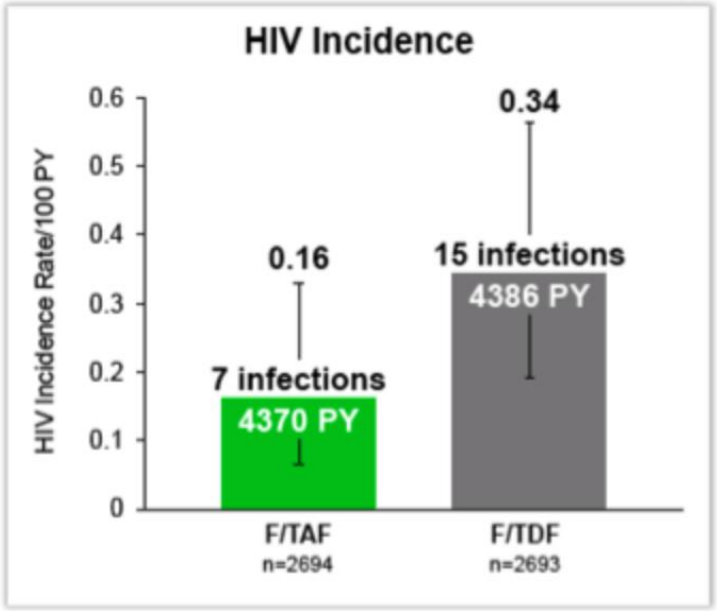


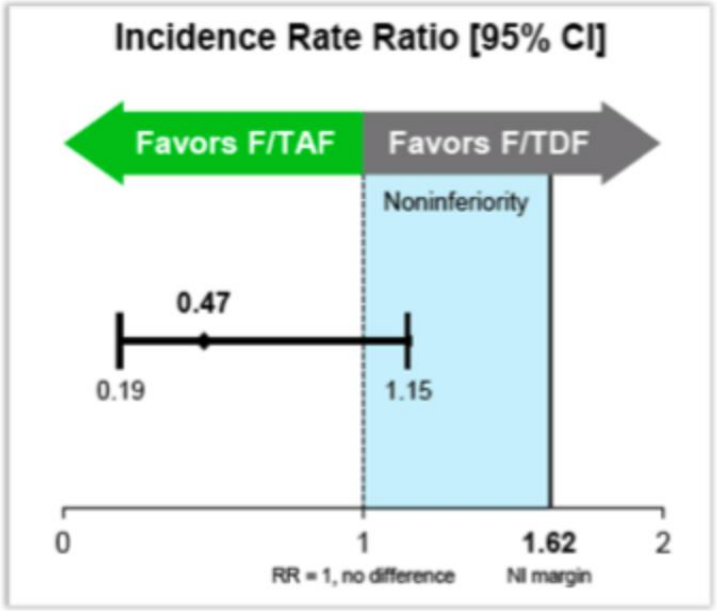
4 pills of TDF/FTC taken over 3 days to cover one sexual intercourse

Discover Trial

DISCOVER Primary Endpoint Analysis: HIV Incidence

22 HIV infections in 8756 PY of follow-up





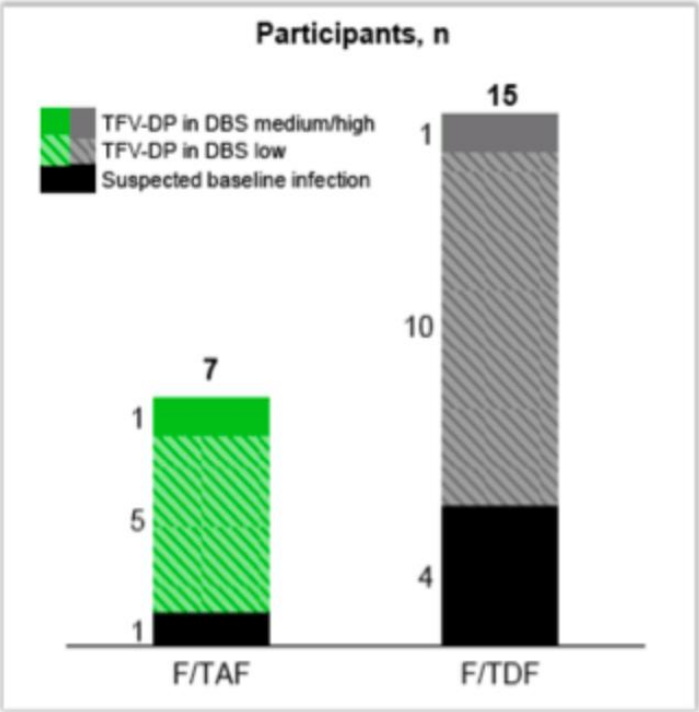
F/TAF is noninferior to F/TDF for HIV prevention

CI, confidence interval; RR, rate ratio.

Hare, CROI 2019

Discover Trial

DISCOVER Adherence and Resistance Analyses of HIV Infections



- 7 F/TAF infections: 1 suspected baseline infection, 5 low levels of TFV-DP in DBS,1 medium level
- 15 F/TDF infections: 4 suspected baseline infections, 10 low levels of TFV-DP in DBS, 1 high level
- In a sensitivity analysis that excluded suspected baseline infections, noninferiority was maintained (0.55 [0.20, 1.48])

n	F/TAF n=7	F/TDF n=15
Resistance genotyped*	6	13
Resistance to study drugs		
FTC	0	4†
TFV	0	0

*3 samples could not be amplified; †All 4 participants with resistance were suspected baseline infections.

Hare, CROI 2019

Case 3

Corey, 48 y/o, MSM presenting for initial PrEP evaluation. 1 reported partner within the past year without condoms. Diagnosed with Strep pharyngitis after development of fevers/chills, night sweats and prescribed amoxicillin/clavulanate. Developed rash after 3 days that worsened after antibiotic discontinuation. He was hospitalized and a drug allergy was diagnosed. HIV test in hospital was non-reactive.

Lab	Result
POC HIV 1/2 Ag/Ab Test	Reactive Ab; p24 Ag faintly reactive
CMP	ALT 71; all others normal
HBV s Ag/Ab, c Ab	All non-reactive
HCV Ab	Non-reactive
STI screenings (G/C, Syphilis)	All Negative

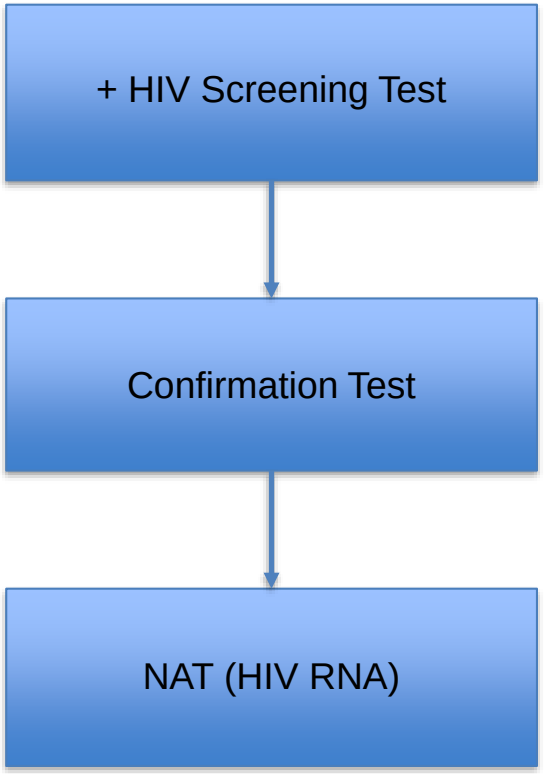
Case 3

Corey, 48 y/o, MSM, with acute viral symptoms, 1 partner, no condoms, reactive HIV Ab, faintly reactive HIV Ag, CMP unremarkable, non-reactive HBV/HCV serology's, negative STI screenings

What is the most appropriate next step for Corey based on his history and labs?

1. Collect baseline HIV labs
2. Collect baseline HIV labs and start bictegravir/emtricitabine/tenofovir AF
3. Collect HIV confirmatory testing and HIV RNA
4. Start emtricitabine/tenofovir DF
5. Have Corey return in 4 weeks for a repeat POC HIV test

Is That Real?



<u>False Positive Reasons:</u>

- Auto-antibodies
- Vaccinations
- Viral infection

<u>Ambiguous Results:</u>

1. Continue PrEP
2. Add additional antiretroviral agent
3. Discontinue PrEP

Smith et al, *Open Forum Infect Dis*, 2018

Case 4

TK, 19 y/o male, presents to clinic asking for nPEP. TK reports anal intercourse and the condom broke. TK is an established patient and is in good health.

What baseline labs would you get prior to starting nPEP?

1. Blood chemistries
2. HIV screening test
3. Hepatitis B serologies
4. STI screening
5. All of the above

Case 4

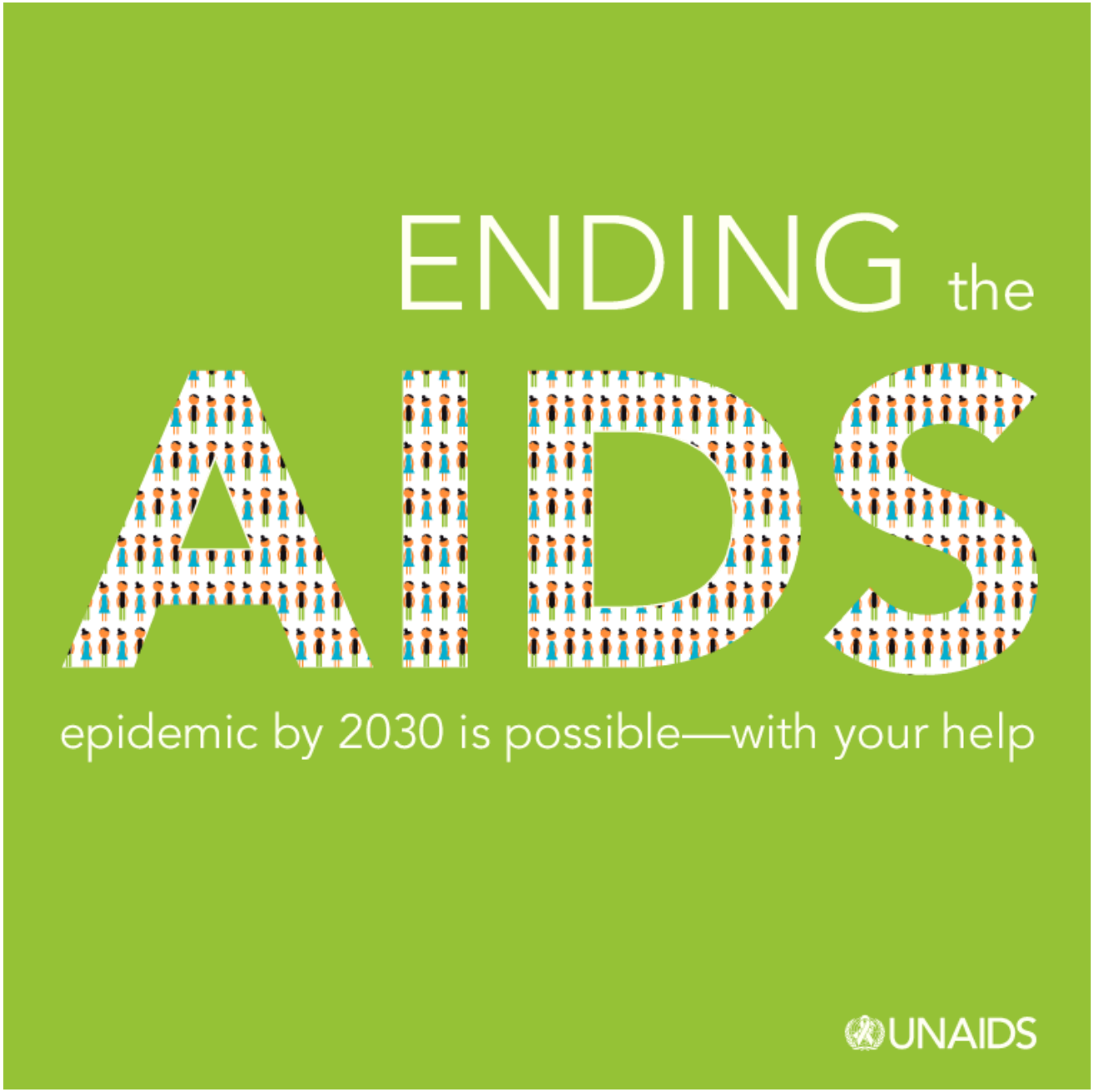
TK, 19 y/o male, presents back to clinic 1 month later for nPEP follow-up. TK reports 20 partners with minimal condom usage in the past 6 months. Most partners are random that he meets off Grindr and he sometimes uses meth and poppers during sexual encounters.

What should be offered to TK? *Select all that apply*

1. Continuation of nPEP for 4 weeks
2. Valacyclovir for genital herpes prophylaxis
3. PrEP
4. Strict risk reduction counseling
5. HPV vaccination series
6. Substance use treatment

Summary

1. PrEP works
2. It is relatively easy to incorporate and manage
3. Access to PrEP in the Midwest is limited
4. Challenges still arise with implementation and scale up
5. Many opportunities exist


ENDING the
AIDS
epidemic by 2030 is possible—with your help
UNAIDS

Resources

Local:

- Sara Bares, MD sara.bares@unmc.edu
- Josh Havens, PharmD jhavens@unmc.edu

National:

- PrEPline Phone Consultations through UCSF Clinical Consultation Center
    - (855) HIV-PREP; Mon-Fri 9am-8pm EST

University of Nebraska Medical Center

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