

Phillip Peters, M.D.
Office of AIDS Medical Center, Department of Public Health

Effective November 7, 2018, Dr. Phil Peters was appointed as the Medical Officer for the California Department of Public Health's Office of AIDS. Dr. Peters graduated from Cornell University Medical College and completed his internal medicine residency and infectious disease fellowship at Massachusetts General Hospital and Emory University, respectfully. Prior to working at the office of AIDS, he joined the Centers for Disease Control and Prevention (CDC) as an epidemic intelligence service (EIS) officer in 2006 and initially led projects evaluating HIV antiretroviral therapy in clinics supported by the President's Emergency Plan for AIDS Relief (PEPFAR). At CDC, Dr. Peters also led several HIV outbreak responses to identify and interrupt large or unusual clusters of HIV infections. In 2015, he led CDC's field investigation team during the largest US HIV outbreak in 20 years, which occurred among people who inject drugs in a rural community. This response interrupted further HIV transmission in the community and resulted in significant federal and state public health policy changes related to injection drug use. At the Office of AIDS, Dr. Peters is working on expanding access to HIV pre-exposure prophylaxis in addition to HIV molecular epidemiology, support for the AIDS Drug Assistance Program, and evaluation of clinical services provided by the Ryan White Part B program.

Dr. Peters is board certified in internal medicine and infectious disease medicine and has remained clinically active working on the infectious disease consult service. He is a volunteer clinical faculty member at the University of California at Davis's department of infectious disease. Dr. Peters is also a member of the immunization panel for the US "Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents" and has served as a study investigator for the National Institute on Drug Abuse's (NIDA) rural opioid project and the AIDS Clinical Trials Group's early HIV treatment study.

HIV Pre-exposure Prophylaxis (PrEP):

A Clinical Overview of HIV Prevention

Philip Peters, MD
Office of AIDS Medical Officer

May 10, 2019
Medical Board of California
Executive Committee



Disclosures

- Dr. Peters has no relevant financial affiliations to disclose

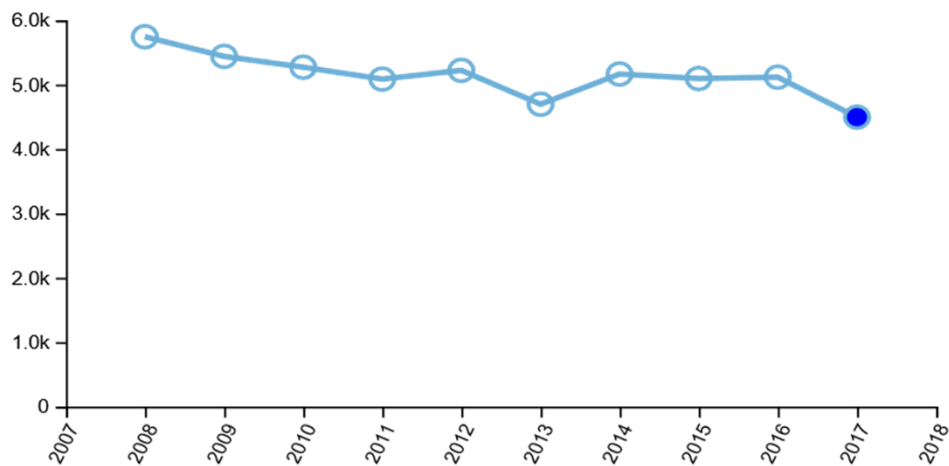


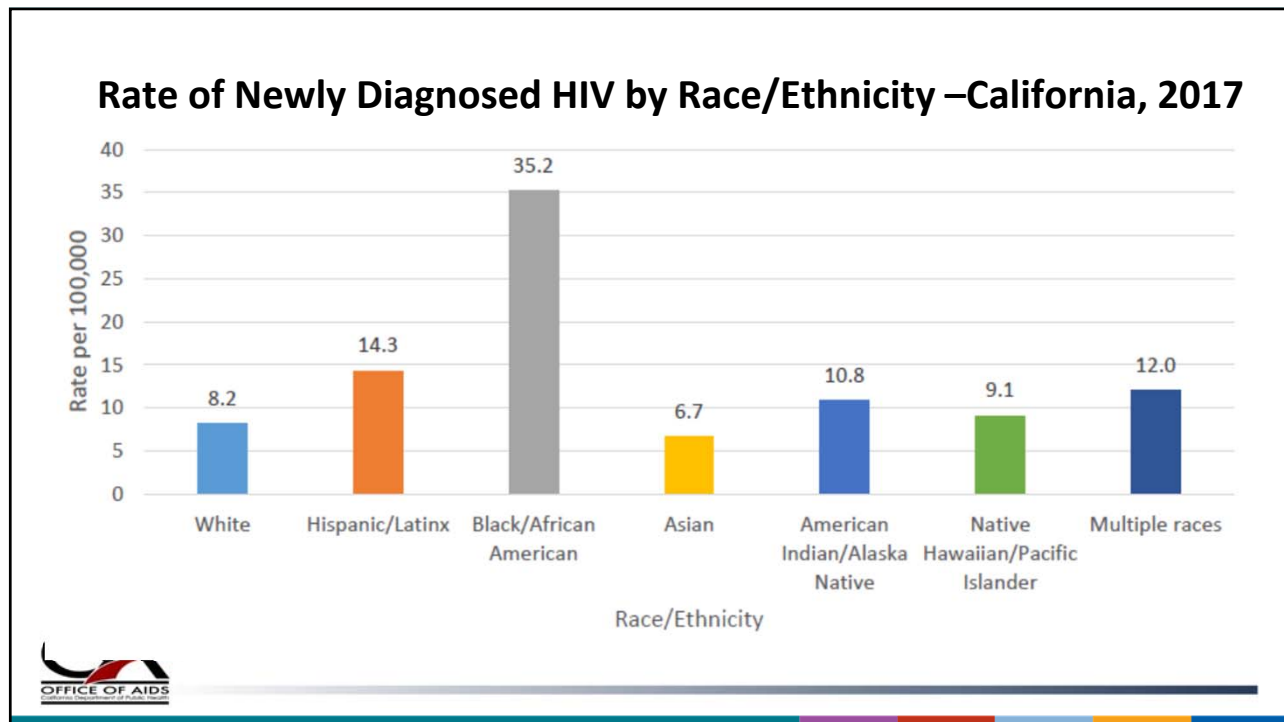
Objectives

- Efficacy and safety of PrEP
- Recommendations for PrEP initiation and monitoring
- Novel PrEP agents and dosing strategies in phase 3 trials
- Patient access and financial support
- PrEP utilization in California and nationally
- Expanding access to PrEP



People diagnosed with HIV infection in California, 2007 – 2017





PEP vs. PrEP

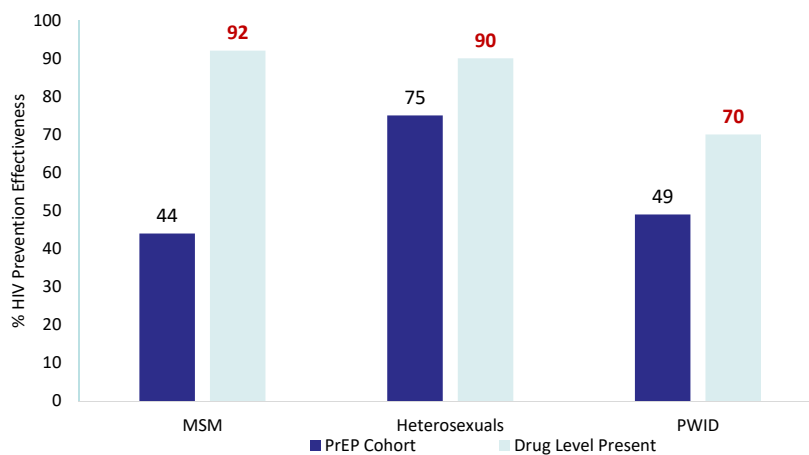
- **Post-exposure Prophylaxis: PEP**
 - 28-day course of a 3-drug antiretroviral regimen to help prevent HIV acquisition; given ≤ 72 hours after an exposure that presents a substantial risk for HIV transmission
- **Pre-exposure Prophylaxis: PrEP**
 - Daily oral fixed-dose combination antiretroviral medication to reduce the risk of HIV acquisition, taken for during a period of risk (e.g. months to years)

PrEP

- **Food and Drug Administration (FDA) approved once-daily pill containing a fixed-dose combination of two antiretrovirals:**
 - Tenofovir disoproxil fumarate (TDF) 300 mg
 - Emtricitabine (FTC) 200 mg
- **Brand name: Truvada**
- **Approved for PrEP in 2012**



Daily oral PrEP effectiveness by adherence in initial randomized trials



Sources: Grant RM et al. N Engl J Med. 2010;363:2587-99; Baeten JM, et al. N Engl J Med. 2012;367:399-410; Choopanya K, et al. Lancet. 2013;381: 2083-90

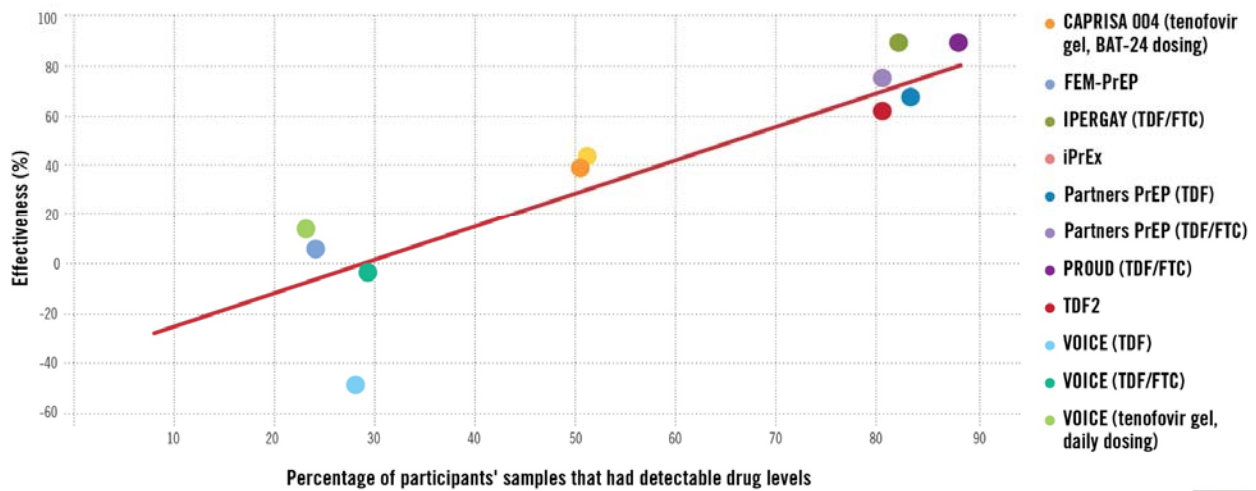
PrEP effectiveness by adherence in open-label and observational studies

Intervention	Prevention effectiveness	Adherence by drug level testing
MSM (iPrEx OLE, TDF/FTC)	0 seroconversions with protective drug levels	Protective drug levels found at 33% of visits
Heterosexual discordant couples (Partners PrEP OLE, TDF/FTC)	96% reduction from expected incidence	2 seroconversions in inconsistent PrEP users, neither with positive partners on ART
MSM (NIAID Demo Project, TDF/FTC)	0 seroconversions with protective drug levels	80% with protective drug levels at 48 weeks
MSM (Kaiser SF, TDF/FTC)	0 seroconversions over 388 persons/years of PrEP use	-



Sources: Grant RM et al. Lancet Infect Dis, 2014; 14:820–9, Baeten JM et al. PLoS Med. 2016;13(8):e1002099; Liu AY et al. JAMA Intern Med. 2016;176 (1):75-84; Marcus JL et al. J Acquir Immune Defic Syndr. 2016;73(5):540-546

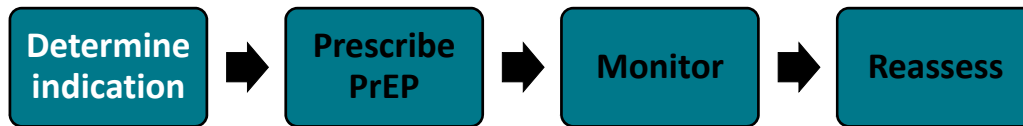
PrEP Works if You Take It — Effectiveness and Adherence in Trials of Oral and Topical Tenofovir-Based Prevention



<https://www.avac.org/infographic/effectiveness-and-adherence-trials-oral-and-topical-tenofovir-based-prevention>



PrEP Steps



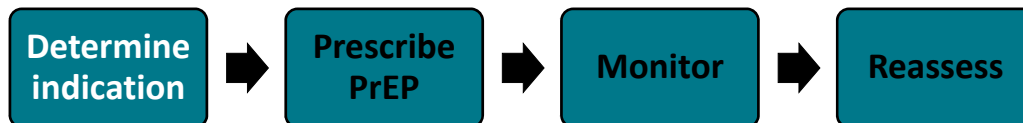
1. Identify patients who may benefit from PrEP

- People who ask for PrEP
- People with HIV-positive partners
- People with sexual exposures including anal sex
- People with bacterial sexually transmitted infection (STI)
- People who inject drugs (PWID)



• Quick Clinical Guide: HIV PrEP Pre-Exposure Prophylaxis (PDF): <https://www.cdph.ca.gov/Programs/CID/DOA/Pages/OAadap.aspx#prep>
 • Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2017 Update. Clinical Practice Guideline. US Public Health Service. <https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf>

PrEP Steps



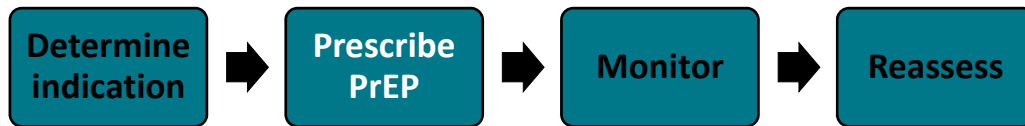
2. Discuss PrEP including potential risks and benefits

- Potential side effects
- Adherence and foreseeable barriers
- Risk of resistance with acute HIV infection
- Time to protection



• Quick Clinical Guide: HIV PrEP Pre-Exposure Prophylaxis (PDF): <https://www.cdph.ca.gov/Programs/CID/DOA/Pages/OAadap.aspx#prep>
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PrEP Steps



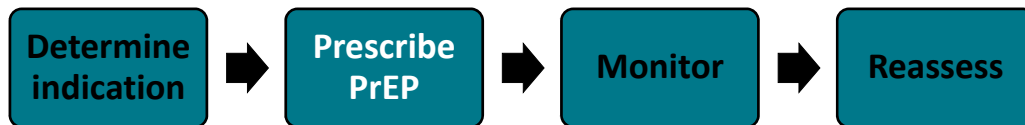
3. Obtain baseline history, ROS, and testing

- HIV antigen/antibody test +/- HIV RNA test
- Serum Creatinine
- Hepatitis B surface antigen and Hepatitis C antibody
- STI testing (based on patient sexual practices)
- Pregnancy test (when appropriate)



• Quick Clinical Guide: HIV PrEP Pre-Exposure Prophylaxis (PDF): <https://www.cdph.ca.gov/Programs/CID/DOA/Pages/OAadap.aspx#prep>
 • Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2017 Update. Clinical Practice Guideline. US Public Health Service. <https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf>

PrEP Steps



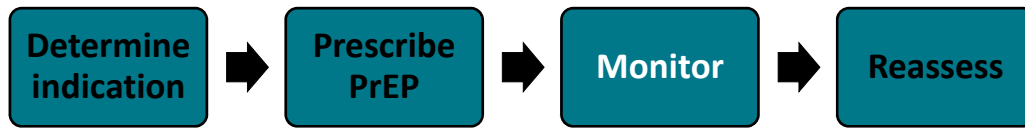
4. Initiate PrEP

- Same-day PrEP prescriptions when possible
- 30-day supply with 0-2 refills for first dispensation
- Adherence counseling and anticipatory guidance
- Counsel on risk reduction and using condoms



• Quick Clinical Guide: HIV PrEP Pre-Exposure Prophylaxis (PDF): <https://www.cdph.ca.gov/Programs/CID/DOA/Pages/OAadap.aspx#prep>
 • Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2017 Update. Clinical Practice Guideline. US Public Health Service. <https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf>

PrEP Steps



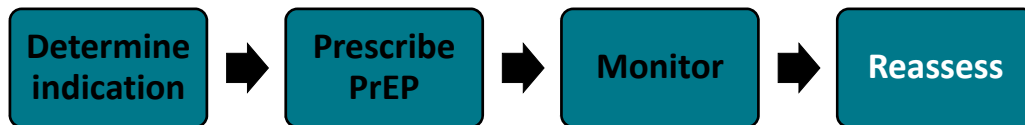
5. Monitor and provide ongoing support

- At 30 days assess side effects and adherence
- Every 3 months HIV, STI, and other testing



• Quick Clinical Guide: HIV PrEP Pre-Exposure Prophylaxis (PDF): <https://www.cdph.ca.gov/Programs/CID/DOA/Pages/OAadap.aspx#prep>
 • Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2017 Update. Clinical Practice Guideline. US Public Health Service. <https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf>

PrEP Steps



6. Reassess ongoing need for PrEP

- If tests positive for HIV, transition immediately to treatment
- If patient wants to discontinue, document HIV status and creatinine and discuss HIV prevention plan

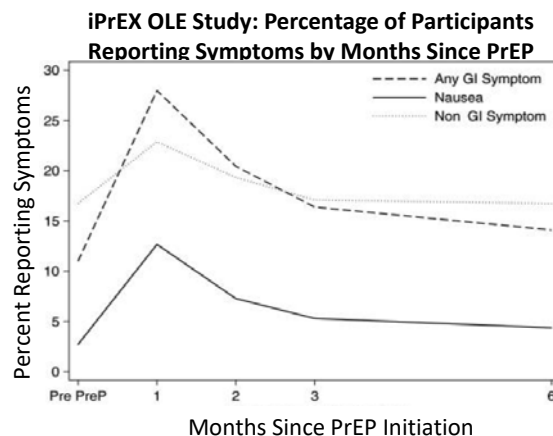


• Quick Clinical Guide: HIV PrEP Pre-Exposure Prophylaxis (PDF): <https://www.cdph.ca.gov/Programs/CID/DOA/Pages/OAadap.aspx#prep>
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Adverse effects and common concerns

▪ Start up syndrome

- Some people using PrEP have mild to moderate symptoms: nausea, vomiting, headache
- Symptoms peak in first month, resolve for most by 3 months



Sources: Grant R et al. N Engl J Med. 2010;363:2587; Glidden et al. Clin Infect Dis. 2016 May 1; 62(9): 1172–1177

Adverse effects and common concerns

▪ Renal

- Tenofovir associated with nephrotoxicity in HIV-infected patients; incidence of 1.09 per 1000 person-years
- In PrEP trials 1-2% of treatment group developed creatinine elevation, not statistically different than placebo group
- Normalization of creatinine levels after PrEP discontinued
- Creatinine monitoring is recommended



Sources: Medland NA et al. Int J STD AIDS. 2018;29(3):227-236; Riddell J et al. JAMA. 2018; 319(12):1261-1268

Adverse effects and common concerns

▪ Bone density

- Some studies have reported small, subclinical decreases in bone mineral density while taking PrEP
- Decrease of 1-2% bone mineral density with no concurrent increase in fractures
- Evidence that changes are reversible after PrEP discontinuation
- No recommendation for routine bone mineral density monitoring



Sources: Liu AY et al. PLoS One 2011; 6:e23688; Kasonde M et al. PLoS One 2014; 9:e90111; Fonner et al. AIDS. 2016 Jul 31;30(12):1973-8; Mirembe BG et al. J Acquir Immune Defic Syndr 2016; 71:287–294

Adverse effects and common concerns

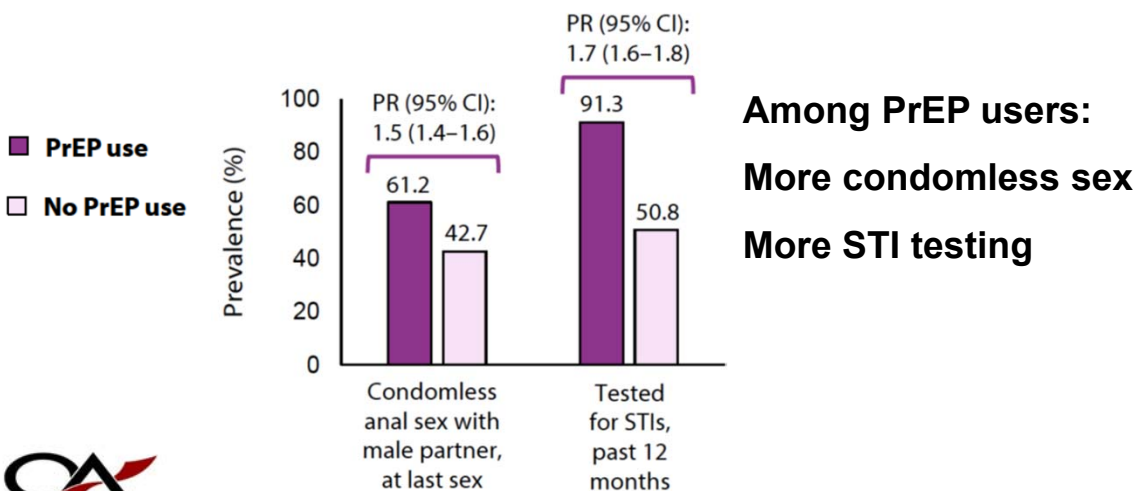
▪ Resistance

- Acute HIV infection at PrEP initiation:
 - For those started on PrEP when acutely infected, risk of resistance is significantly higher in PrEP versus placebo groups (risk ratio=3.34, 95% CI: 1.11–10.06, P=0.03)
 - Manage risk by excluding acute HIV infection at the time of PrEP initiation



Sources: Fonner et al. AIDS. 2016 Jul 31;30(12):1973-8

Condomless Sex and STI Testing Among MSM by PrEP Use in Past 12 Months



CDC National HIV Behavioral Surveillance: Chapin-Bardales et al., abstract #968, CROI 2019, Seattle WA

PrEP Risk versus Benefit Summary

U.S. Preventive Services TASK FORCE

You are here: Home » Public Comments and Nominations » Opportunity for Public Comment » Draft Recommendation Statement : Draft Recommendation Statement

Draft Recommendation Statement
Prevention of Human Immunodeficiency Virus (HIV) Infection: Pre-Exposure Prophylaxis
 This opportunity for public comment expired on December 26, 2016 at 8:00 PM EST

Note: This is a Draft Recommendation Statement. This draft is distributed solely for the purpose of receiving public input. It has not been disseminated otherwise by the USPSTF. The final Recommendation Statement will be developed after careful consideration of the feedback received and will include both the Research Plan and Evidence Review as a basis.

Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

Population	Recommendation	Grade (What's This?)
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

See the **Clinical Considerations** section for information about identification of persons at high risk and selection of effective antiretroviral therapy.

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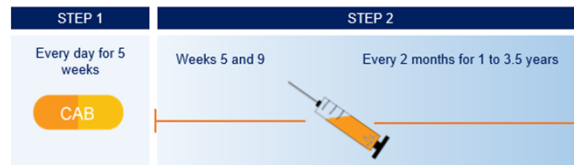
PrEP is an effective and safe therapy for preventing HIV transmission.

Increasing prescription of PrEP for patients at risk of acquiring HIV has the potential to reduce new HIV infections.



Novel PrEP agents in Phase 3 clinical trials (select examples)

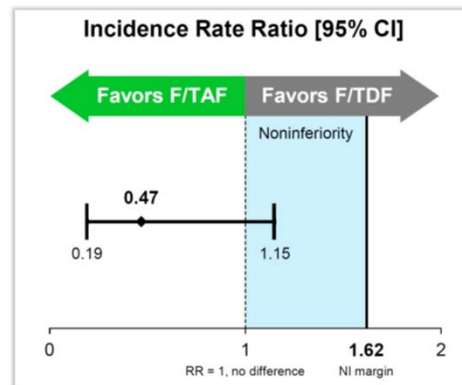
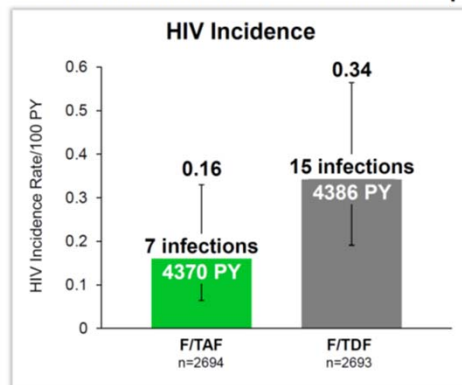
- **Tenofovir alafenamide (TAF) / FTC**
- **Dapivirine ring: ~30% efficacy**
- **Cabotegravir long acting injection**



Sources: Baeten JM et al. N Engl J Med 2016;375:2121-2132; Nel A et al. N Engl J Med 2016;375:2133-2143

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.

9



Hare, CROI 2019, Abstract 104H

PrEP 2-1-1: non-daily PrEP dosing strategy



IPERGAY : Sex-Driven iPrEP

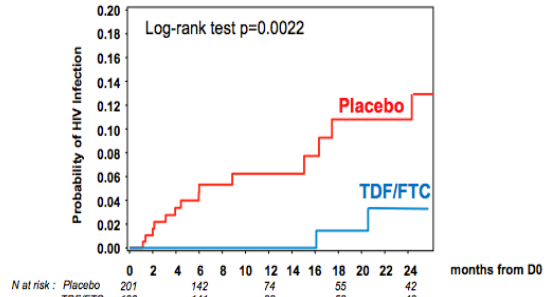
- ✓ 2 tablets 2-24 hours before sex
- ✓ 1 tablet 24 hours later
- ✓ 1 tablet 48 hours after first intake



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



KM Estimates of Time to HIV-1 Infection (mITT Population)



Median follow-up of 9.3 months: 16 subjects infected
14 in placebo arm (incidence: 6.60 /100 PY) and **2 in TDF/FTC arm** (0.91 /100PY)
86% relative reduction in the incidence of HIV-1 (95% CI : 40-98, p=0.002)
NNT to avert one HIV-infection: 18 (95% CI: 11-50)

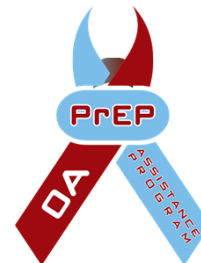
Molina et al NEJM 2015

HOWEVER: median pills=4 doses/week.....

Slide 25 of 65

PrEP Access

- Generally covered by medical insurance plans including Medi-Cal
- Manufacturer patient assistance program
- PrEP Assistance Program (AP)
 - Initiated in 2018 by California to further remove financial barriers and improve access



PrEP-AP

The State of California's assistance program for the prevention of HIV helps cover medical costs related to getting pre-exposure prophylaxis (PrEP)

You may qualify if you are

- A California resident
- Aged 18 or older
- HIV negative
- Have a modified adjusted gross income of \$62,450 or less for a household of one, or \$84,550 or less for a household of two
- Not fully covered by Medi-Cal or other third party payers
- Enrolled in one of Gilead's assistance program (if eligible)



What PrEP-AP Covers*

- ✓ Co-pays for Truvada®
- ✓ Out of pocket costs for PrEP-related medical services such as HIV testing and STI screening
- ✓ Costs for prescriptions (Rx's) on the PrEP-AP formulary

*Not all enrollees qualify for the benefits listed here. For more information see "What to Expect" below.

PrEP-AP Enrollment


- Authorized PrEP-AP enrollment site
- Enrollment Worker determines program eligibility and enroll clients in:
 - PrEP-AP, and
 - Gilead's Patient Assistance Program or
 - Gilead's Co-Payment Assistance Program

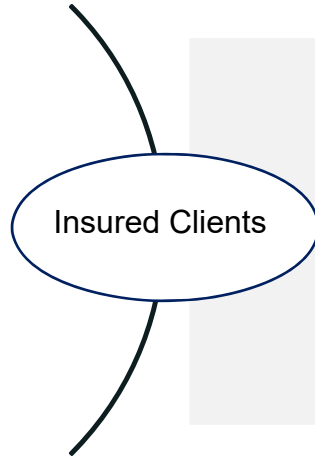
PrEP-AP Uninsured

Uninsured Clients

- Approved PrEP-related medical out-of-pocket costs through the contracted PrEP-AP Provider Network.
- Medications on the PrEP-AP formulary for the prevention of HIV and sexually transmitted infection (STI) treatment, excluding Truvada®



PrEP-AP Insured



- Approved PrEP-related medical out-of-pocket costs
- Will pay the gap between what the client's insurance plan and the manufacturer's co-payment assistance program will pay towards Truvada© for eligible clients (if applicable)
- Medications on the PrEP-AP formulary for the treatment of STIs

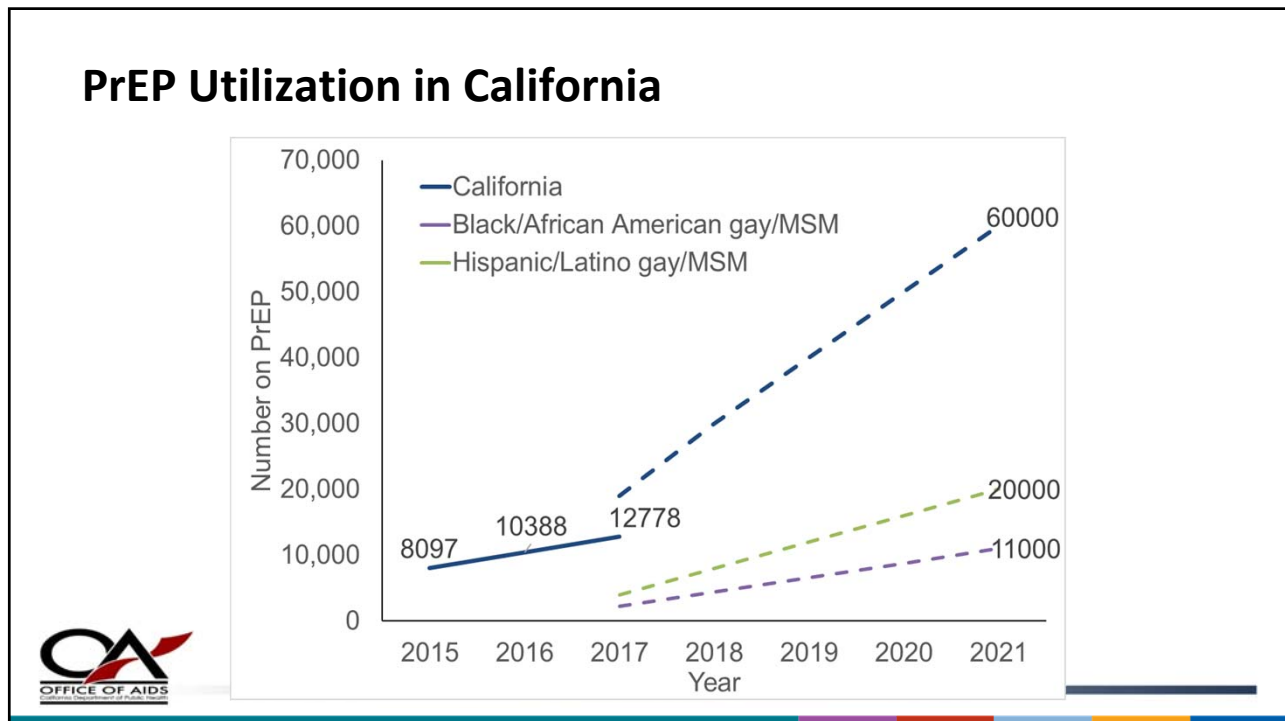
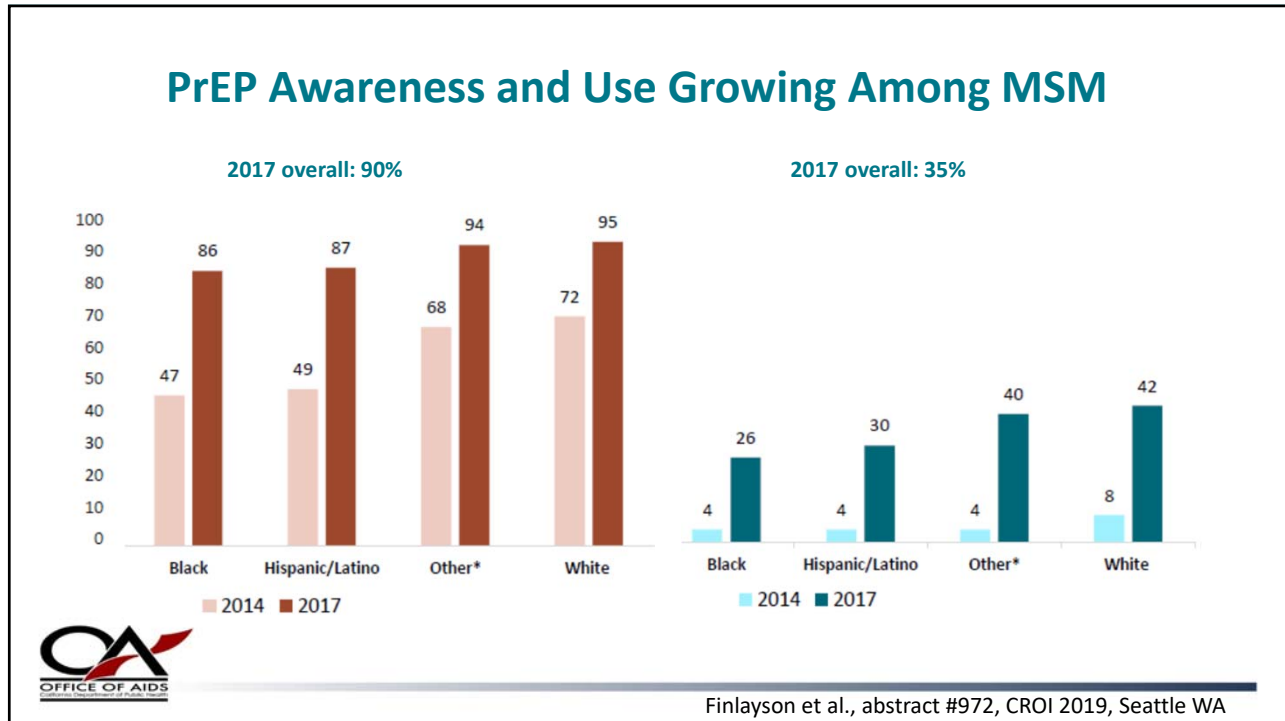


Future of PrEP-AP

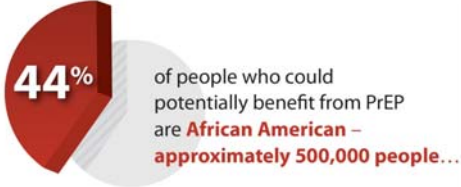
Recent changes in California legislation approved through the 2018 Budget Act will expand the PrEP-AP to include:

1. Payment of post-exposure prophylaxis (PEP) and related medical costs
2. Payment for up to 14 days of PEP and PrEP starter packs
3. Up to 28 days of PEP medication for victims of sexual assault regardless of whether eligibility requirements are met
4. The ability to consider insured individuals as uninsured for confidentiality or safety reasons
5. Access for individuals aged 12-17
6. Gilead co-payment assistance bypass for insured clients when the insurance plan does not accept manufacturer co-payment coupon cards





HIV prevention pill is not reaching most who could potentially benefit – especially African Americans and Latinos



...but only **1%** of those – **7,000 African Americans** – were prescribed PrEP*

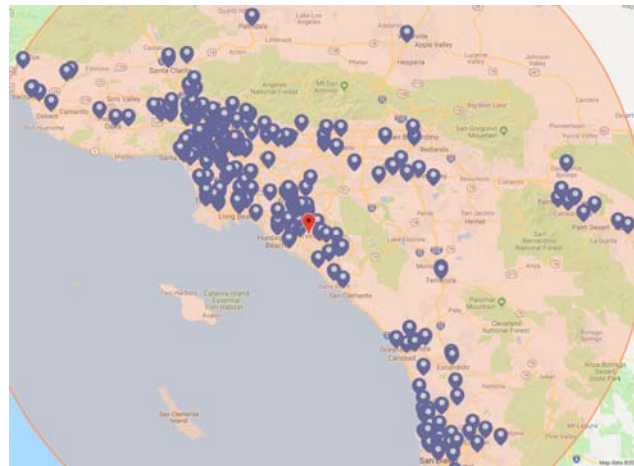
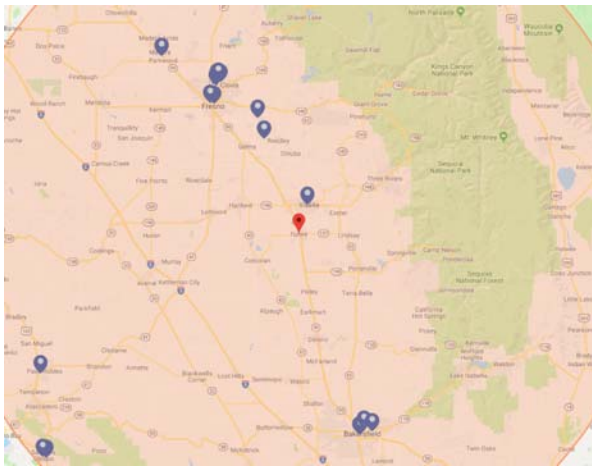


...but only **3%** of those – **7,600 Latinos** – were prescribed PrEP*



*Prescription data in this analysis limited to those filled at retail pharmacies or mail order services from September 2015 – August 2016; racial and ethnic information not available for one-third of the prescription data

PleasePrEPme.org Provider Locator



PrEP: expanding access in California

- **Consumer education**
- **Physician PrEP detailing and consultation**
- **Health department PrEP referrals and navigation**
 - linked to HIV testing, partner notification, and STI treatment
- **State funded community PrEP navigation projects**
- **End the epidemic – HRSA funded community health centers**
- **Telemedicine options**
- **Physician education**



PrEP: expanding access in California

- **PrEP Dear Colleague Letter**
- **Opportunities for Continuing Medical Education (CME) Requirements**
- **Four states have an HIV CME requirement**
- **Straight-forward but evolving medical intervention**
- **Area of significant public health and medical investments**



Acknowledgements

CDPH

- Marisa Ramos
- Sandra Robinson
- Kevin Sitter
- Adrian Barraza

CDC

- Mary Tanner
- Dawn Smith
- Karen Hoover

