DRAFT

HIV PRE-EXPOSURE AND POST-EXPOSURE PROPHYLAXIS FOR CALIFORNIA PHARMACISTS

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AETC AIDS Education & Training Center Program Pacific

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Overview

- Role of pharmacists in HIV prevention
- PREP Basics
- PEP Basics
- Legal Requirements of Furnishing in California
- HIV Testing
- Patient financial considerations
- Cases
  - PREP
  - PEP

ROLE OF THE PHARMACIST IN HIV PREVENTION

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Learning Objectives

- Describe the Care Continuum to measure "Getting to Zero" goals.
- Identify 4 HIV prevention tools available to California pharmacists

NEW CDC GOALS FOR ENDING THE HIV EPIDEMIC: TO REDUCE NEW HIV INFECTIONS 90% BY 2030

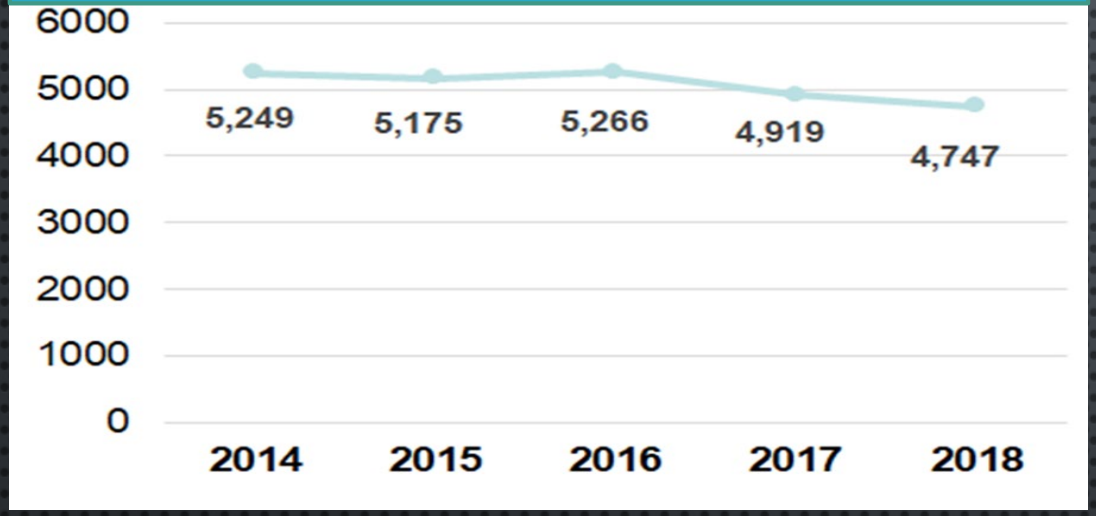
- DIAGNOSE all PLWH (Persons living with HIV) as early as possible
- TREAT PLWH rapidly and effectively to reach sustained viral suppression
- PREVENT new HIV transmissions using proven interventions (e.g. PrEP, U=U** syringe exchange services)
- RESPOND quickly to HIV outbreaks to get needed prevention services to people who need them

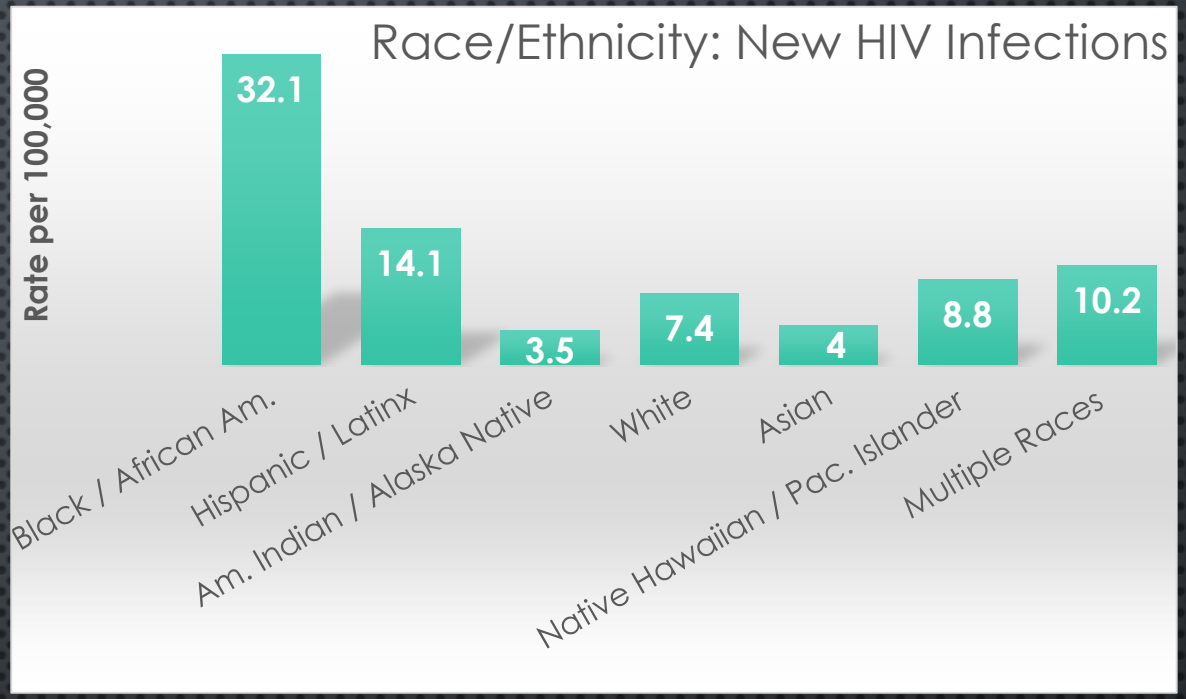
**Undetectable= Untransmittable

https://www.cdc.gov/hiv/policies/strategic-priorities/mobilizing/index.html?ACSTrackingID=USCDC_1046-DM48014&ACSTrackingLabel=HIV%20Prevention%20in%20the%20United%20States%3A%20Mobilizing%20to%20End%20the%20HIV%20Epidemic&deliveryName=USCDC_1046-DM48014

THE HIV EPIDEMIC IN CALIFORNIA 2019

- 137,785 living with HIV
- 4,396 new HIV infections





https://aidsvu.org/local-data/united-states/west/california/

California Department of Public Health, Office of AIDS, California HIV Surveillance Report — 2019.

US AND CA HIV CONTINUUM OF CARE

HIV in the United States

Not all people with HIV are getting the care they need. An estimated **1.2 million people had HIV in the US in 2018**. For **every 100 people with HIV:***

86 received an HIV diagnosis

65 received some HIV care

50 were retained in care

56 were virally suppressed

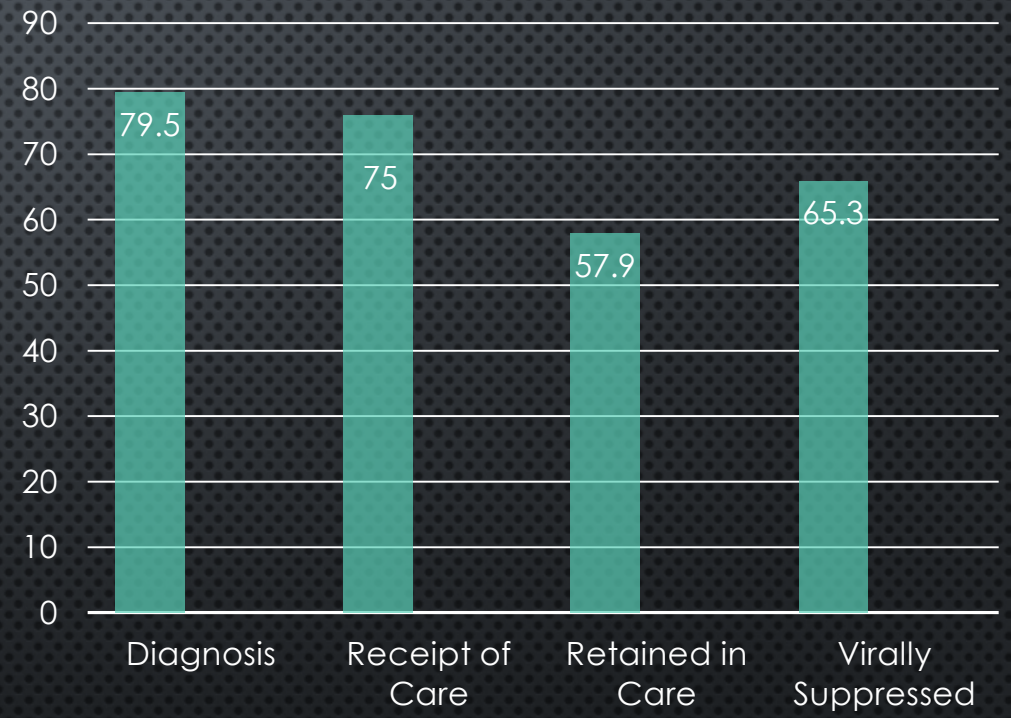
* Includes people with diagnosed or undiagnosed HIV.

www.cdc.gov/hiv | 1-800-CDC-INFO

Get Tested. Get in Care. Stay in Care. Stay Healthy.

Sources: CDC. Monitoring selected HIV prevention and care objectives using HIV surveillance data–United States and 6 dependent areas, 2018. *HIV Surveillance Supplemental Report 2020;25*(2).
CDC. Selected national HIV prevention and care outcomes (slides).
Based on the most recent data available in December 2020.

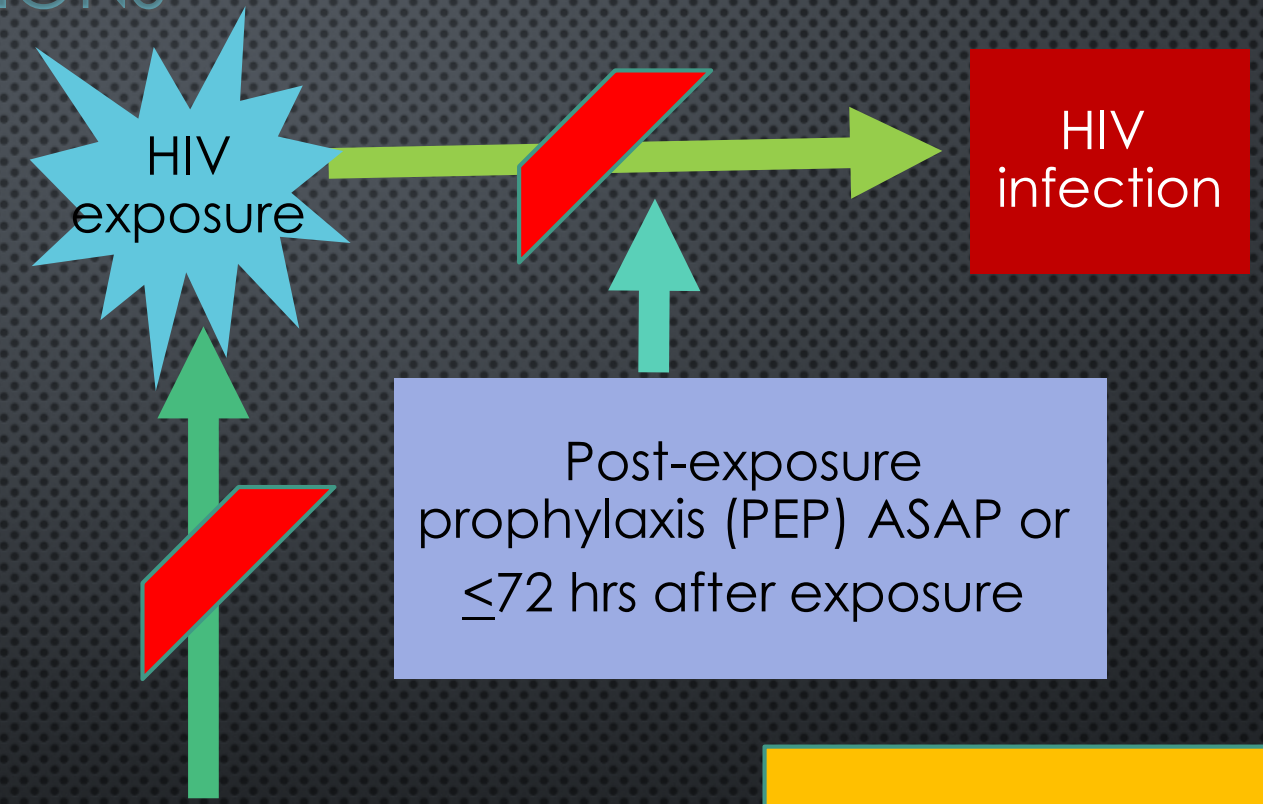
2019 CA Continuum of Care



CDC 2018 Surveillance: https://www.cdc.gov/hiv/statistics/overview/ataglance.html;
CA Dept of Public Health Office of AIDS Surveillance Report 2019 https://www.cdph.ca.gov/Programs/CID/DOA/Pages/OA_case_surveillance_reports.aspx

PRE-EXPOSURE (PREP) AND POST-EXPOSURE (PEP) PROPHYLAXIS CAN PREVENT HIV INFECTIONS

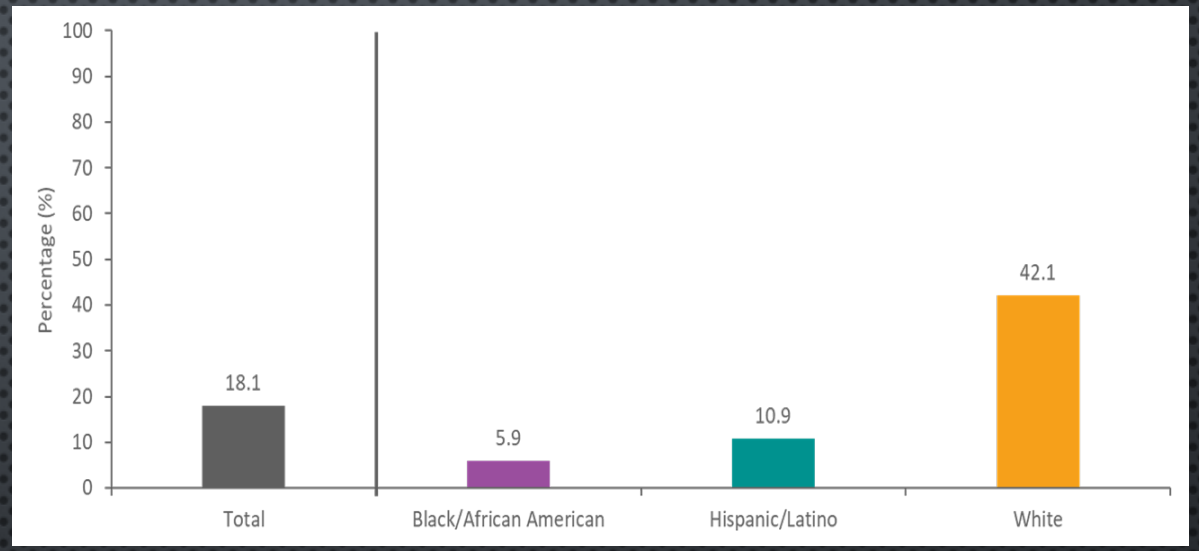
- PRE-EXPOSURE PROPHYLAXIS (PREP) BEGUN BEFORE HIV EXPOSURE CAN PREVENT HIV.
- POST-EXPOSURE PROPHYLAXIS STARTED ASAP AFTER HIV EXPOSURE REDUCES THE CHANCE OF HIV INFECTION
- BEFORE STARTING PREP AND PEP, MUST RULE OUT ACUTE/ESTABLISHED HIV INFECTION.

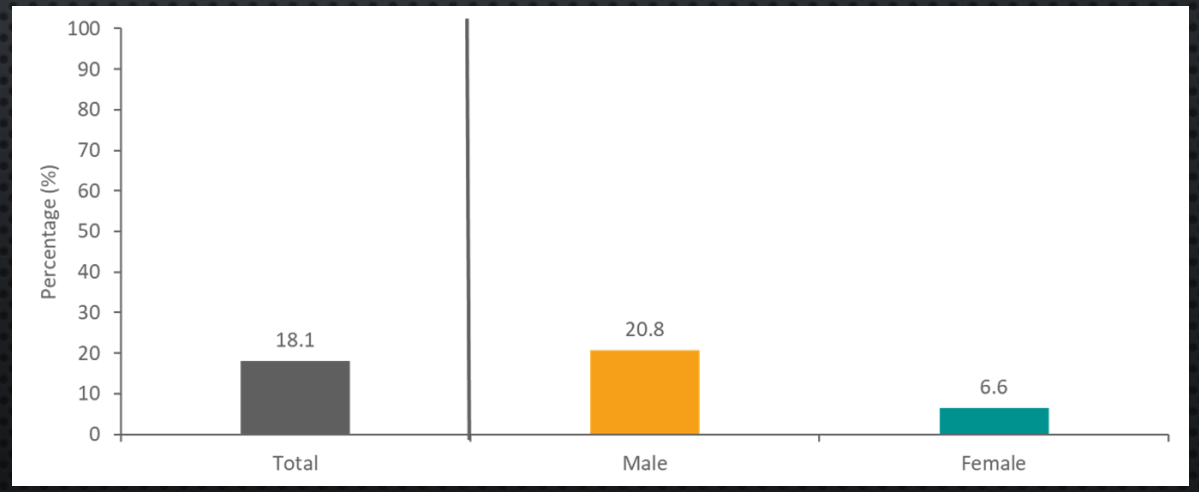


HIV prevention in the United States 2021.
https://www.cdc.gov/hiv/policies/strategicpriorities/mobilizing/index.html?ACSTrackingID=USCDC_1046DM48014&ACSTrackingLabel=HIV%20Prevention%20in%20the%20United%20States%3A%20Mobilizing%20to%20End%20the%20HIV%20Epidemic&deliveryName=USCDC_1046-DM48014

PREP USE AMONG US PERSONS AGED ≥16 YRS, 2018 BY RACE AND SEX

- ONLY 21.9% (~27,283) OF THE ESTIMATED >>1MILLON CALIFORNIANS WHO COULD BENEFIT ARE USING PREP
- PREP IS NOT REACHING MOST VULNERABLE PERSONS WHO COULD POTENTIALLY BENEFIT, ESPECIALLY BLACK, HISPANIC/LATINX, AND WOMEN





https://www.cdc.gov/hiv/library/slidesets/index.html HIV prevention and cares outcome

SB 159: NEW HIV PREVENTION TOOL

- Increasing access to PrEP and PEP in pharmacies can reduce HIV infections in persons at risk.
- Pharmacists can Independently initiate and furnish
  - 30 to 60 days of PrEP once every 2 yrs
  - 28 to 30 days of emergency PEP
- Requires pharmacists to support patient linkage to care for continuous prevention prescriptions
- All pharmacy staff, including clerk, technicians, interns work as a team to support the health of patients.

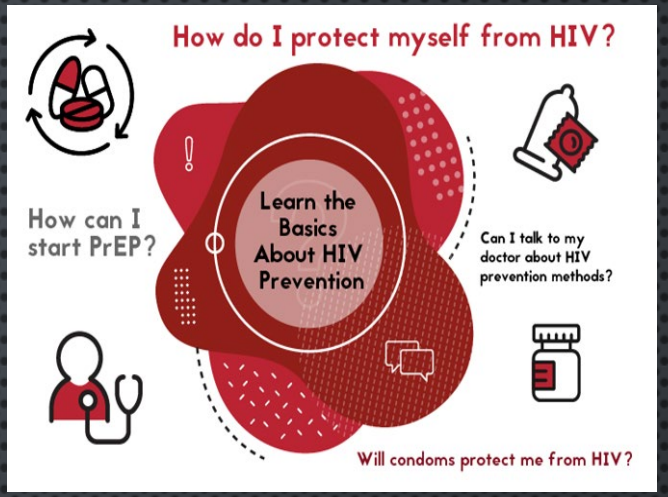
https://www.cdc.gov/stophivtogether/hiv-prevention/prep.html

HIV PREVENTION BY PHARMACISTS

- Pharmacists can optimize comprehensive HIV prevention strategies to prevent HIV Infection and provide harm reduction to optimize PrEP and PEP
  - Condom, Sterile Syringes, Safer Sex
  - Treatment As Prevention: Undetectable = Untransmittable (U=U)
  - Naloxone
- Skills for these services are similar to other public health prevention interventions available by pharmacists:
  - emergency contraception, Immunizations, Tobacco Cessation

CDC Sept 2017 endorses
U=U
Undetectable = Untransmittable

CONCLUSION



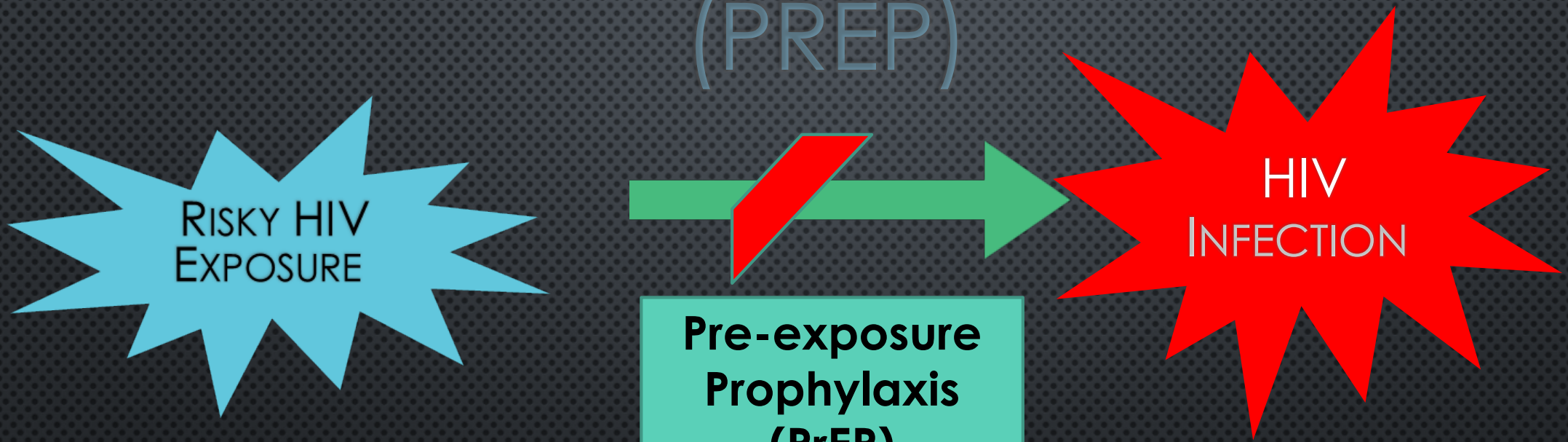
- Pharmacists are trusted, knowledgeable, and accessible health care providers to
  - support CDC and CA HIV Prevention Goals
  - provide access to condoms, sterile syringes & support HIV adherence
  - improve access to PrEP and PEP under SB 159, especially for underserved patients not engaged in care
  - Provide linkage to care for ongoing PrEP prescriptions, HIV testing, and lab monitoring
- pharmacies are ideal locations for emergency access to PEP and to Provide transition to PrEP if appropriate

PRE-EXPOSURE PROPHYLAXIS (PREP) BASICS

Learning Objectives

- Describe the data supporting use of PrEP in HIV prevention
- Use CDC guidelines to identify patients appropriate for starting PrEP medications.
- Counsel patients regarding the importance of confirming negative HIV test prior to starting HIV PrEP.
- Counsel patients regarding dosing and common side-effects for PrEP medications.
- Consider patients appropriate for tenofovir diproxil fumerate (TDF) versus tenofovir alafenamide (TAF) containing PrEP regimens.
- Counsel patients regarding linkage to care and follow-up laboratory monitoring.

PRE-EXPOSURE PROPHYLAXIS (PREP)



Negative HIV test 7 days before starting PrEP

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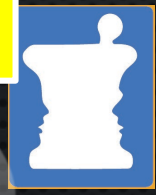
HIV NEGATIVE PERSONS APPROPRIATE FOR PREP

MSM (Men Who Have Sex with Men)	Heterosexual Men and Women	Persons Who Inject Drugs (PWIDs)
• Male partner in last 6 mo. • Not in monogamous relationship **AND one of the following:** • No condoms w/ anal sex in last 6 mo • STI in the last 6 mo • Relationship with HIV positive partner ▪ Transactional sex for money, drugs, housing	• Sex with partner in the last 6 mo • Not in a monogamous relationship **AND one of the following** • Is a bisexual man • Infrequent condom use with ≥1 at-risk partner (e.g. PWIDS, bisexual) • Relationship with HIV+ partner • Bacterial STI in the last 6 mo ▪ Transactional sex for money, drugs, housing	• Injection of non-prescribed drugs ▪ And use of stimulants such as methamphetamines during sex **AND one of the following** • Sharing of injection or drug use equipment in the last 6 mo • Risk of sexual transmission ▪ Transactional sex for money, drugs, and housing

- Persons who request PrEP are also appropriate candidates
- Negative HIV test and no acute HIV symptoms within 7 days of starting PrEP.



Adapted from USPHS Preexposure Prophylaxis for the Prevention of HIV Infection in the United States—2017 update.

Assess for acute HIV symptoms

- Within 2 to 4 weeks after HIV infection, about 2/3 will have a flu-like symptoms.
  - Fever
  - Chills
  - Rash
  - Night sweats
  - Muscle aches
  - Sore throat
  - Fatigue
  - Swollen lymph nodes
  - Mouth ulcers
- last from few days to several weeks. Some are asymptomatic
- Refer persons with these symptoms for HIV RNA testing and supportive care.
- Provide education that persons are infectious for HIV transmission during acute/chronic phases of infection
- Recommend safer sex, condom use to prevent sexual transmissions

FDA APPROVED DRUGS FOR PREP

**Both FDA indicated for Hep B therapy

Drugs/Dosage	Brand	FDA PrEP Indications	Not Recommended
FTC/TDF or F/TDF (Emtricitabine 200 mg plus tenofovir disoproxil fumarate 300mg) One tablet daily with or without food	Truvada, Generic	All HIV-**negative** adults: [men who have sex with men (MSM), persons who inject drugs (PWIDs), discordant heterosexual men/women, transgender men and women**] **and** adolescents ≥ 35 kg(77lb)	CrCL <60ml/min ? Childs Pugh class C liver impairment
FTC/TAF or F/TAF (Emtricitabine 200 mg + tenofovir alafenamide 25 mg) One tablet daily with or without food	Descovy	2019: HIV **negative** MSM and transgender women** having sex with men and adolescents ≥ 35 kg (77lb)	Avoid in receptive vaginal sex (cis-women, transgender men), PWIDs -CrCL < 30 ml/min -CrCL <15 cc/min unless on dialysis -?? Childs Pugh class C liver impairment -P4503A inducers

** **transgender: sex at birth differs from their self-identified gender and lifestyle**

Clinical Trials of TDF/FTC Efficacy as PrEP

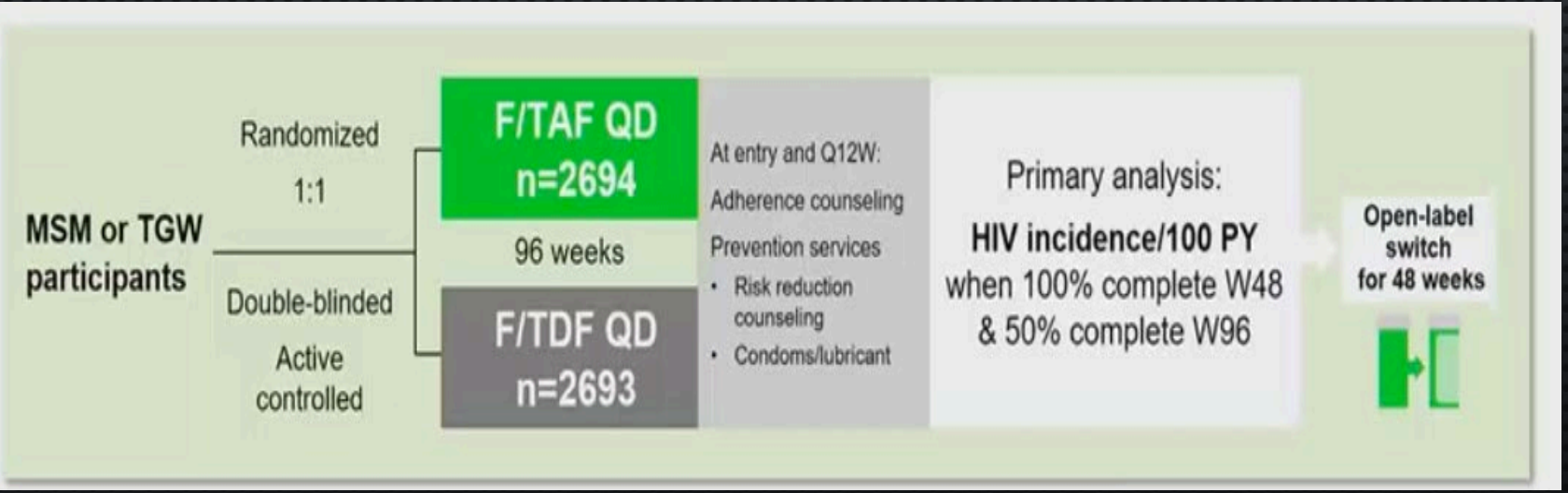
Clinical trial	Participants	Number	Drug	% reduction in HIV infections		Adjusted efficacy based on TDF detection in blood [c]
				%	(95% CI)	%
iPrEx	MSM, trans women	2499	F/TDF	44	(15-63)	44
Partners PrEP	HIV discordant couples	4747	TDF	67	(44-81)	81
			F/TDF	75	(55-87)	90
TDF 2	Heterosexually men & women	1219	F/TDF	62	(22-83)	79
Bangkok	IDU	2413	TDF	49	(10-72)	67
PROUD	MSM	545	F/TDF	86	(58-96)	100
IPERGAY	MSM	400	"on demand"	86	(40-99)	86
Kaiser	MSM	972	F/TDF	100		92
Fem-PrEP	Heterosexually active women	1951	F/TDF	NS	-----	37
VOICE	Heterosexually active women	5029	F/TDF	-49	-----	29
ATN 110	Young MSM 17-22 yrs old	200	F/TDF	HIV 3-6%		56% (4wks) 34% (48wks)

Adherence is essential for PrEP efficacy

US Public Health Services. Preexposure Prophylaxis For The Prevention Of HIV Infection In The United States, 2014, Hosek SG et al. JAIDS 2017;74:21.

F/TAF VS F/TDF FOR HIV PREVENTION: DISCOVER TRIAL

- Comparing FTC/TAF to FTC/TDF in men & transgender women (N=5387) who have sex with men (MSM) X 96 weeks. Excellent adherence (96-98%)
- One HIV+ infection in each group (FTC/TAF non-inferior to FTC/TDF)
- FTC/TAF had better bone and renal outcomes
- TAF/FTC NOT FDA approved in cis-women or transgender men for receptive vaginal sex. No data in PWIDs
-



Mayer KH et al, Lancet 2020; 396

Tenofovir and Emtricitabine (FTC) Pharmacology

- Both Tenofovir DF and AF formulations and emtricitabine (FTC) are Nucleoside Reverse Transcriptase Inhibitors (NRTIs) that inhibit
  - HIV reverse transcriptase enzyme to blocks further HIV viral replication
  - HBV polymerase to block HBV replication
- Converted intra-cellularly to tenofovir diphosphate (TDF-DP) & emtricitabine triphosphate (FTC-TP)
  - 90% higher tenofovir plasma levels with TDF than TAF
  - Lower TAF plasma levels: ↓ risk of renal dysfunction and bone loss
- combined with 3 or more antiretrovirals to treat HIV infection

TENOFOVIR AND EMTRICITABINE PHARMACOLOGY

- ACTIVE AGAINST HEPATITIS B VIRUS (HBV).
- HBV SCREENING REQUIRED AS PART OF BASELINE LABORATORY TESTS TO EXCLUDE UNDERLYING HBV INFECTION
- COUNSEL PATIENTS WITH CHRONIC HBV INFECTION NOT TO STOP PREP UNLESS ADVISED BY THEIR PRIMARY CARE PROVIDER.
- ABRUPT DISCONTINUATION OF PREP IN PERSONS WITH CHRONIC HBV INFECTION CAN CAUSE HBV FLARES, LIVER DYSFUNCTION, AND SIGNIFICANT MORBIDITY.
- CHRONIC HBV INFECTION IS NOT A CONTRAINDICATION TO PREP

TIME TO MAXIMUM PROTECTION FOR TDF

- TIME FROM STARTING DAILY ORAL DOSES OF F/TDF TO MAXIMAL HIV PROTECTION IS UNKNOWN AND VARIES BY SITE OF EXPOSURE.
- PHARMACOKINETIC STUDIES IN HIV NEGATIVE PERSONS PROVIDE PRELIMINARY DATA ON TIME TO ACHIEVE STEADY STATE TDF-DP IN BLOOD, MONONUCLEAR CELLS, RECTAL, VAGINAL TISSUES.
- GIVING A DOUBLE DOSE INITIALLY OF TDF/FTC MAY REDUCE TIME TO PROTECTION, ESPECIALLY IN MSM
- PENETRATION INTO GENITAL SECRETIONS: RECTAL >> CERVIX/VAGINAL

Daily F/TDF 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

PrEP Precautions, Warnings, Adverse Effects

- Safe and well tolerated
- Start up Syndrome: self limiting
- Stopping due to ADRs rare (<2%)
- Warnings and precautions
  - Adverse drug reactions (ADRs): kidney, bone mineral density, metabolic
  - lactic acidosis, hepatomegaly with steatosis
- BLACK Box Warnings:
  - Severe acute HBV exacerbations reported in HBV-infected persons who stopped PrEP
- Drug resistance (<0.1%) following undetected acute HIV infection

PrEP Start Up Syndrome

- 1-18% of persons starting PrEP
  - GI: (nausea 4-5%, diarrhea 5-6%), < 2%: headache, fatigue, abdominal pain/discomfort, flatulence
  - Usually transient and self limiting (1-3 weeks but can be prolonged , up to 3 months in studies)
- Counseling:
  - Temporary, improves with time
  - Supportive care
    - Take with food, ginger, crackers, etc, prn nausea
    - Short term APAP/NSAIDs prn headache, pain, fatigue
    - Hydration to replace fluids prn vomiting
    - Anti-motility agents, BRATT diet if diarrhea

PREP SAFE & WELL TOLERATED BUT REQUIRES ROUTINE MONITORING

Adverse Effects	TDF/FTC	TAF/FTC	Recommendation
Renal dysfunction	▪ ↓ eGFR 1-5 ml/min, ▪ ↑ proteinuria, Fanconi syndrome (rare) ▪ Delayed onset (55+/-28 mo) ▪ ↑ risk if age > 40 yrs old, CrCl < 90 cc/min, DM, HBP, ↑ high dose/frequent NSAIDS ▪ Avoid if CrCl ≤ 60cc/min	▪ ↑eGFR 1.8 ml/min ▪ ↓ proteinuria/Scr ▪ Fanconi syndrome not reported ▪ Avoid if CrCL< 30 cc/min unless on dialysis	▪ Monitor BUN/Scr every 3 months ▪ Maintain hydration ▪ Avoid high dose NSAIDS, nephrotoxins
Bone Mineral Density (BMD)	▪ ↓ BMD in 1-2 yr ↓0.99% hip; 1.12% spine BMD ▪ No ↑ risk of fractures ▪ Back to baseline BMD if d/c ▪ Consider F/TAF if appropriate	▪ stable hip, ↑spine 0.5% BMD ▪ No ↑ risk of fractures	▪ Lab/DXA not recommended unless osteoporosis or osteopenia. • ↑bone health (↓smoking, ETOH, ↑CA, exercise)

Expert Opinion on Safety 2016; USPSTF *JAMA*. 2019;321(22):2203-22; Mayer H et al. Lancet 2020; 396:239

PREP SAFE & WELL TOLERATED BUT REQUIRES ROUTINE MONITORING

Adverse Effects	TDF/FTC	TAF/FTC	Recommendation
Lipids and weight	▪ Lipids: ↓ median TC –0.28; LDL –0.18, HDL -0.13 mmol/L ▪ Weight ↓ mean 0.1 kg/no change	▪ Lipids: Median TC -0.03, LDL+ 0.03, HDL –0.05 mmol/L ▪ Weight ↑1.1 to 1.3 kg/yr	▪ No change in TC/HDL ratio so unclear CV risk ▪ Maintain healthy weight, diet, exercise
Pregnancy and Breast feeding	▪ 1st trimester TDF exposure (class B) suggest no risk of poor birth outcomes or delays in infant growth ▪ Minute levels in breast milk	▪ Limited data ▪ TAF/FTC in 2nd trimester with good birth outcomes.	▪ Pregnancy test ▪ TDF/FTC safe during ▪ preconception and pregnancy

Mugwanya, Baeten Expert Opinion on Safety 2016; USPSTF *JAMA*. 2019;321(22):2203-22; Mayer H et al. Discover trial; Lancet 2020; 396:239,

PREP DRUG INTERACTIONS REQUIRES ROUTINE MONITORING

	F/TDF	F/TAF
Mechanism	-Drugs that reduce renal function or compete for tubular secretion may ↑ TDF -some Hep C drugs may ↑TDF renal dysfunction	-Drugs that reduce renal function or compete for tubular secretion ↑TAF -P-gp inhibition can ↑ TAF -P-gp induction can ↓ TAF
Drug Interaction (examples)	-high dose or multiple NSAIDs -ledipasvir/sofosbuvir -velpatasvir/sofosbuvir -velpatasvir/voxilaprevir/sofosbuvir	-high dose or multiple NSAIDs -aminoglycosides <u>Selected 3A4/P-gp Inducers:</u> ↓ TAF Carbamazepine/Oxcarbazepine Anticonvulsants: phenytoin, phenobarbital Herbals: St. John's Wort Rifampin, rifabutin, rifapentine

Liverpool HIV Drug Interaction https://www:hiv-druginteractions.org/

Other Treatment Considerations

- PrEP does not prevent STI: ↑ frequency STI Observed
  - Gonorrhea and Chlamydia – Urine, rectal swabs, throat swabs Q 3mo or if symptoms
  - Syphilis – RPR q 3 mo or if symptoms
  - Educate and recommend condoms
- Hepatitis C: ↑ risk MSM and PWIDs: HCV Ab baseline and yearly
- Hepatitis B: baseline serology (HBsAG, HBcoreAB, HBsAB)
  - Vaccinate if not immune and ensure immunity
  - Risk of HBV flare/↑ liver function tests if PrEP stopped in persons with underlying HBV infection
  - HBV is not a contraindication to Prep

PREP WORKFLOW

- Identify Persons who could benefit from or request PrEP
- Provide Confidential pharmacy area for sensitive discussions
- Ask about interest, readiness, and understanding about using PrEP
- Confirm HIV negative status within 7 days of prep start and no signs of acute HIV infection
- Counsel about daily adherence, time to protection, side effects
- offer adherence support (i.e. phone app)

PrEP Workflow

- Provide referral/list of local PrEP providers, local DPH for laboratory assessment (STI, HBV, HCV, renal) and ongoing prescriptions.
- Dispense at least 30 days of PrEP
- Enroll in Patient Assistance Program for copay support if uninsured
- Bill Medi-Cal for Counseling Services
- At 30 day refill, confirm linkage to care, assess adherence
- Can dispense another 30 day of PrEP if good adherence and linked to care

SUMMARY: PREP

- Approx 99% effective in sexual exposures and 70% in PWIDS with good adherence
- Longer and more experience with F/TDF: uncommon and delayed toxicities
- TAF/FTC ONLY studied/FDA approved in MSM/transgender women.
  - Avoid in women and transgender men having receptive vaginal sex and in persons who inject drugs (PWIDS) until data is available
  - Less renal and bone effects but more weight gain and ↑ cholesterol
  - May be preferred in >40 years old, DM, HTN, CrCL <90 cc/ml, Osteoporosis
  - Drug Interactions with 3A4/PgP inducers (e.g. anticonvulsants)
- SB159 PREP for 30-60 days duration safe for majority of recipients

Conclusion

Pharmacists have:

- the training and expertise to support persons who need PrEP.
- The skills to counsel about the importance of PrEP adherence

- Pharmacists can
  - Identify and collaborate with PrEP providers to begin PrEP
  - Identify HIV testing programs and ability to provide CLIA-waived tests
  - Confirm HIV negative status within 7 days before starting PrEP
  - Link patients to care for laboratory monitoring of STI, renal function, HCV, HBV status as well as on-going prescriptions.

SELECTED PREP RESOURCES FOR HEALTH CARE PROVIDERS

- CLINICAL QUICK GUIDE TO PREP HTTPS: CLINICAL QUICK GUIDE TO PREP - CDPH - CA.GOV
- CDC GUIDELINES HTTPS://WWW.CDC.GOV/HIV/CLINICIANS/PREVENTION/PREP-AND-PEP.HTML
- PACIFIC AIDS EDUCATION AND TRAINING CENTER HTTP://PAETC.ORG/
- NATIONAL CLINICIANS CONSULTATION CENTER: PRE-EXPOSURE PROPHYLAXIS TELEPHONE CONSULTATION 1-855 448-7737 OR (855) HIV-PREP)HTTPS://NCCC.UCSF.EDU/

California Department of Public Health https://cdph.ca.gov

- Liverpool HIV Drug Interactions https://www.hivdruginteractions.org/
- University of Washington HIV Curriculum https://www.hiv.uw.edu/
- Health HIV https://healthhiv.org/

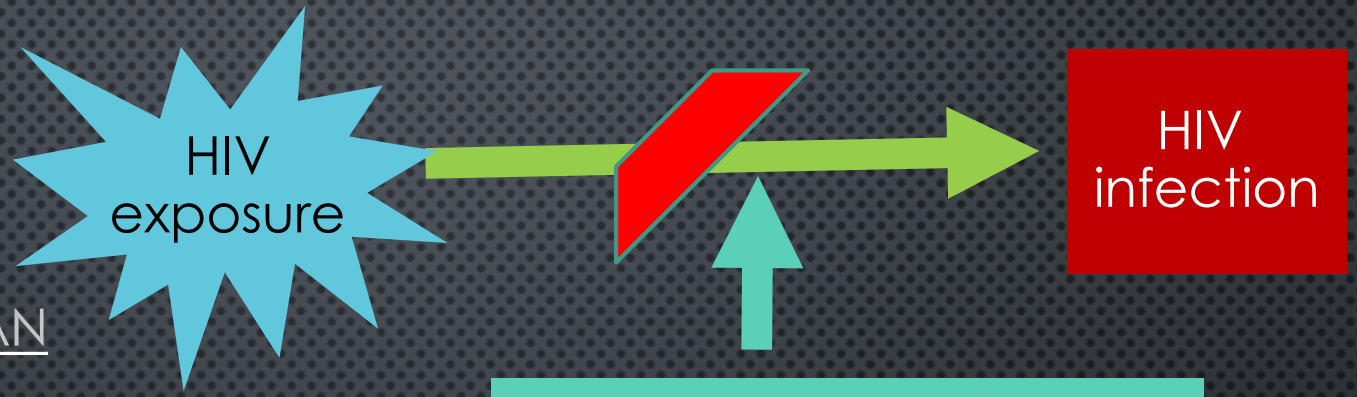
POST-EXPOSURE PROPHYLAXIS (PEP)

Learning Objectives

- Identify patients who can benefit from Post-Exposure Prophylaxis (PEP) for HIV
- Choose a PEP regimen appropriate for the patient
- Effectively counsel patients about the risk of HIV infection after exposure and benefit of PEP
- Link patients to care for follow-up testing and support following HIV exposure.

POST-EXPOSURE (PEP) PROPHYLAXIS FOR PREVENTING HIV INFECTION

- POST-EXPOSURE PROPHYLAXIS STARTED ASAP BUT NO LATER THAN 72 HR AFTER HIV EXPOSURE REDUCES THE CHANCE OF HIV INFECTION
- BEFORE STARTING PEP, MUST RULE OUT ACUTE/ESTABLISHED HIV INFECTION.



Post-exposure prophylaxis (PEP) ASAP or ≤72 hrs after exposure

Before prescribing PEP, it is critical to rule out acute HIV infection

HIV prevention in the United States 2021.
https://www.cdc.gov/hiv/policies/strategicpriorities/mobilizing/index.html?ACSTrackingID=USCDC_1046DM48014&ACSTrackingLabel=HIV%20Prevention%20in%20the%20United%20States%3A%20Mobilizing%20to%20End%20the%20HIV%20Epidemic&deliveryName=USCDC_1046-DM48014

ESTIMATED PROBABILITY OF ACQUIRING HIV

Type of Exposure	Risk per 10,000 Exposures
Sexual	
Receptive Anal Intercourse	138
Insertive Anal Intercourse	11
Receptive Penile-Vaginal Intercourse	8
Insertive Penile-Vaginal Intercourse	4
Insertive or Receptive Oral Intercourse	low
Parenteral	
Blood Transfusion	9,250
Needle Sharing During Injection Drug Use	63
Percutaneous Needle Stick	23
Mucous membrane	9
Mother to Child Vertical Transmission	2260

Patel P et al. AIDS 2014; 28:1509; CDC.gov; Baggaley RF et al. AIDS 2006;20;805

WHO ARE POTENTIAL PEP CANDIDATES?

Sites of Exposure	Exposure to:	Assessment	PEP Recommendation
—Receptive vaginal, anal sex —Insertive anal, vaginal sex —Sexual assaults	Semen, vaginal secretions, rectal secretions	-HIV+ or HIV+ risk factors -Receptive vaginal and anal higher HIV risk than insertive penile or anal	-HIV+, recommend -Consider/offer if PEP benefits > risks of HIV infection
—Oral sex	Saliva, ejaculate	-Low risk -Receptive greater than insertive oral sex	-Not warranted -Consider/offer if receptive oral sex with ejaculation, ulcerations, sores, or blood
—Mucous membranes splash	Eyes, mouth	-HIV+ or HIV+ risk factors -Blood or visibly bloody fluids	-HIV+, recommend -If visible blood, consider/offer -Not warranted if no visible blood
—Non-intact Skin (Breaks in skin)	Blood or visibly-bloody body fluids	-HIV+ or HIV+ risk factors	-HIV+, recommend -Not warranted if no blood -Not warranted if intact skin
—Percutaneous contact (e.g. found needle, Persons who inject drugs (PWIDS)	Blood or visibly-bloody body fluids	-HIV+ or HIV+ risk factors	-High risk, recommend -Low risk, offer/consider for found needle

Adapted from CDC Updated Antiretroviral Guidelines after Sexual, Injection drug use, or other Non-occupational to HIV-US2016

Pediatric Considerations

- Primarily considered during sexual assault situations
- Adolescents ≥35kg would be dosed as adults
- Pediatric ARV use may need dosage adjustments, available in Pediatric ARV guidelines (https://clinicalinfo.hiv.gov/en/guidelines/pediatric-arv/overview-0?view=full)
- These doses are not included in legislation under SB159 currently
  - Can refer to emergency room, who also have sexual assault support services

RECOMMENDED PEP REGIMENS X 28 DAYS

PEP Regimens	Dosage X 28 days	Selected Side Effects (SE)
Emtricitabine 200 mg (FTC)/tenofovir disoproxil fumarate 300 mg (TDF) Truvada®, generic **PLUS** Raltegravir (RAL, Isentress®) 400mg TAB or HD 600 mg TAB **OR** Dolutegravir (DTG, Tivicay®) 50 mg TAB	TDF/FTC:1 tablet po daily with or without food if CrCL ≥60ml/min. Use TAF/FTC if CrCL ≥ 30ml/min. RAL 400 mg po BID or RAL HD 2 X 600 mg tabs (1200 mg) daily with or without food. DTG 50 mg po daily with or without food.	Nausea, fatigue, headache (HA), diarrhea, flatulence. Nausea, Headache, insomnia, dizziness, myalgias, ↑ liver function tests Nausea, headache, ↑ serum creatinine (Scr) due to reduced Scr secretion
Fixed dose combination TAB Biktarvy® (FTC 200 mg/TAF 25mg bictegravir (BIC)50 mg)*	1 tablet orally once daily with or without food if CrCL ≥ 30 ml/min *added to CA PrEP AP Formulary 10/2019	Nausea, vomiting fatigue, diarrhea ↑ liver function tests, ↑ Scr
Darunavir (DRV, Prezista®) 800 mg TAB plus Ritonavir (RTV, Norvir®)100 mg TAB if concern about HIV resistance	One tablet each of darunavir and ritonavir given together with food.	Nausea, HA, diarrhea, ↑ lipids, rash if severe sulfa allergy. More SE than RAL or DTG.

Adapted from CDC Updated Antiretroviral Guidelines after Sexual, Injection drug use, or other Non-occupational to HIV-US2016

SELECTED PEP DRUG INTERACTIONS

PEP Regimens	Selected Drug Interactions (DI)
Emtricitabine 200 mg (FTC)/tenofovir disoproxil fumarate 300 mg (TDF) Truvada®, generic Emtricitabine 200 mg (FTC) Tenofovir alafenamide (TAF) 25 mg (Descovy®)	Avoid high dose NSAIDS ↓ TAF levels (e.g. 3A4/P-gp Inducers): anticonvulsants (e.g. carbamazepine, Oxcarbazepine, phenytoin, phenobarbital) St. John's Wort, rifampin, rifabutin, rifapentine
Raltegravir (RAL, Isentress®) 400mg TAB or HD 600 mg TAB	Avoid co-administration of Al/Mg antacids Avoid co-administration Ca carbonate only with HD RAL
Dolutegravir (DTG, Tivicay®) 50 mg TAB	Take DTG 2 hr before or 6 hr after Al/Mg antacids Take calcium and DTG together with food
Fixed dose combination TAB Biktarvy® (FTC 200 mg/TAF 25mg/bictegravir 50 mg	Take Biktarvy® 2 hr before or 6 hr after Al/Mg antacids Take Biktarvy® and calcium together with food
Darunavir (DRV, Prezista®) 800 mg TAB plus Ritonavir (RTV, Norvir®)100 mg TAB	Monitor for 3A4 drug interactions (e.g. fluticasone, statins, agents for erectile dysfunction, antidepressants, rifamycins, anticonvulsants, etc)

Liverpool HIV Drug Interactions: https://www.hivdruginteractions.org

PEP: Counseling and Linkage to Care

- Link Patient to provider to provide f/u HIV, HBV, HCV and STI testing.
- require both baseline and repeat HIV/HCV testing following 28 day PEP regimen.
- Counsel about common/ transient side-effects: nausea, bloating, diarrhea, flatulence, headache
  - Take with food, use ginger-containing food/beverages, dietary changes
  - Take NSAIDS or APAP for headaches
  - Anti-diarrheals prn diarrhea
- Integrase Inhibitors and Polyvalent cation Drug Interactions
- adherence: Pill box, alarm, phone reminder apps, connect to daily routine

PEP WORKFLOW

- Evaluate risk of HIV transmission and benefit of PEP
- document time of exposure is within window for PEP (ASAP but <72 hrs)
- Assess for Acute HIV Symptoms
- Select and dispense 28 day supply of appropriate PEP regimen ASAP
  - do not delay PEP to order medication.
  - Access Patient Assistance Programs for uninsured or copay assistance
- Counseling
  - risks and benefits of PEP
  - adherence and side-effect management
  - link to care for laboratory testing
  - Pep to prep transition for eligible persons

Conclusion

- Pharmacists have the skills and training to:
  - provide timely access to Post-Exposure Prophylaxis (PEP)after risky exposures to HIV ASAP but no later than 72 hrs after exposure.
  - link patients to providers for baseline and follow-up testing for HIV, sexually transmitted diseases, and bloodborne pathogens (e.g. HCV, HBV).
  - select an appropriate PEP regimen and immediately dispense 28 days for hiv prevention.
  - counsel patients about adherence, side-effects, linkage to care and potential transition of PEP to PrEP if eligible

SELECTED PEP CLINICAL RESOURCES FOR HEALTH CARE PROVIDERS

- CDC Guidelines
  https://www.cdc.gov/hiv/clinicians/prevention/prep-and-pep.html
- Non-occupational PEP Guideline
  https://stacks.cdc.gov/view/cdc/38856
- NIH Guidelines
  https://aidsinfo.nih.gov/guidelines
- National Clinicians Consultation Center Post Exposure Telephone Consultation Services
- 1-888-448-4911
  - https://nccc.ucsf.edu/

California Department of Public Health https://cdph.ca.gov

- Pacific AIDS Education and Training Center
  http://paetc.org/
- Liverpool HIV Drug Interactions
  https://www.hivdruginteractions.org/
- University of Washington HIV Curriculum
  https://www.hiv.uw.edu/
- Health HIV https://healthhiv.org/

LEGAL REQUIREMENTS OF FURNISHING IN CALIFORNIA

Learning Objective

- Define key aspects of legislation authorizing pharmacists to furnish PrEP and PEP in California

PREP

Prior to furnishing, a pharmacist must complete a 90 min training program approved by the board

PREP

Furnishing restrictions: At least a 30-day to 60-day supply under specified conditions

- Documented negative HIV test within 7 days before starting PrEP
- No reported signs or symptoms of acute HIV infection
- No reported contraindicated medications
- Mandatory counseling and pharmacy documentation

- CDC Guidelines PrEP – 2017 Preexposure Prophylaxis for the Prevention of HIV Infection in the United States-2017 Update: A clinical Practice Guideline (www.cdc.gov)

PEP

Furnishing Restrictions:

- Patient evaluation to determine if exposure occurred within the previous 72 hour Window
- Patient meets clinical criteria in CDC Guidelines
- HIV testing is provided under CLIA provision
- Mandatory counseling
- Notification to Primary Care Provider

- CDC Guidelines PEP – Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV-United States, 2016

HIV TESTING

Learning Objectives

- Determine recommended HIV test based on clinical circumstances
- Identify pathway for testing outside traditions Settings

HIV TESTING REQUIREMENTS IN SB159

- HIV testing is one important part of the Laboratory testing recommended in CDC guidelines (Links provided)
- timely testing and treatment, as applicable, is also recommended for renal function, hepatitis B, hepatitis C, sexually transmitted diseases, and pregnancy
- testing could occur at or be arranged by the pharmacy or the clinical location where long-term follow-up care will occur
- Pharmacies are encouraged to establish protocols where this testing will occur

HIV TESTING FOR PREP AND PEP

	Timing of Test	Testing Location	Follow-up testing
PrEP	negative HIV test within 7 days before starting PrEP	Patient bring documentation of test or be tested at the pharmacy	Recommend HIV testing every 3 months
PEP	PEP is considered an emergency and can be started before HIV testing	HIV testing can occur at the pharmacy or at a referral site	HIV testing in 4 to 6 weeks and repeat at 12 to 16 weeks

OPTIMAL HIV TESTS FOR DIFFERENT SITUATIONS

Testing Situation	Recommended Test	Comments
HIV exposure in last month or symptoms of acute HIV	HIV RNA PCR (viral load) and HIV antigen/antibody test	If HIV infected – consider rapid HIV treatment
Normal	HIV antigen/antibody test (4th generation) - preferred HIV antibody only testing is an alternative	Lab-based is more sensitive than rapid CLIA waived tests
"Stay-at-Home" Order; in-person visits limited	FDA-approved in-home HIV antibody test on oral fluid*	Less sensitive but an option during the pandemic

* CDC Dear Colleague Letter: https://www.cdc.gov/hiv/policies/dear-colleague/dcl/051520.html

HIV TESTING IN NON-CLINICAL SETTINGS

- Multiple CLIA waived HIV tests are commercially available for rapid testing to facilitate the provision of PrEP and PEP in pharmacy settings
- Pharmacists are authorized to perform CLIA waived tests in accordance with the federal Clinical Laboratory Improvement Amendments of 1988 (42 U.S.C. Sec. 263a) and as specified in California Business and Professions Code (BPC 1206.5)
- Other pharmacy personnel can perform CLIA waived HIV testing after receipt of test counselor training and meeting requirements as specified by California Health and Safety Code (HSC) 120917

PATIENT FINANCIAL CONSIDERATIONS

LEARNING OBJECTIVES

- DISTINGUISH REIMBURSEMENT RESOURCES FOR INSURED AND UNINSURED INDIVIDUALS

Financial Considerations

- Two categories of PrEP and PEP costs
  - PrEP and PEP medication cost including copays
  - Out-of-pocket fees for clinic visit, laboratory testing, and medications to treat common sexually transmitted infections
- Costs coverage require combining insurance and assistance plans

Program	PrEP/PEP medication coverage	Clinic and lab testing
Comprehensive insurance plans (including Medi-Cal)	Yes, PrEP copays to be removed by end of 2020	Covered, may have copay
Manufacturer patient assistance	Yes (full coverage)	No
Federal Ready, Set, PrEP program	PrEP only (full coverage)	No
California PrEP Assistance Program	Covered in select situations when not covered by other programs	Yes (full coverage)

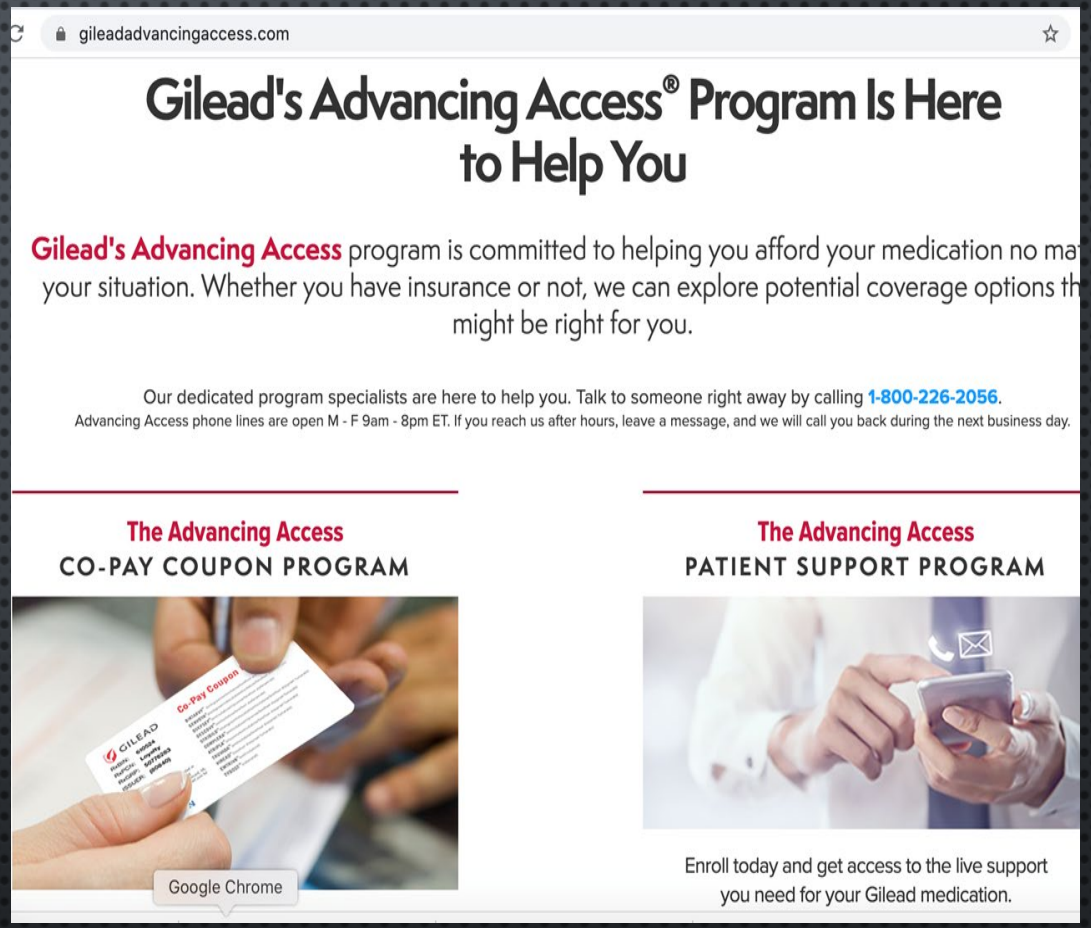
Third Party Reimbursement

- Comprehensive insurance, Medi-Cal, and Medicare cover PrEP and PEP
- PrEP copays are removed from most plans starting in 2021
- May have copays for clinic and lab testing
- SB 159 eliminated prior authorizations for PrEP and PEP
- United States Preventive Services Task Force (USPSTF) issued a grade "A" recommendation for PrEP for persons at high risk of HIV(June 2019)
- Patient Protection and Affordable Care Act (PPACA) states a medical insurer must cover, and may not impose any cost sharing requirement for, any evidence-based preventive items or services that have a grade of "A" or "B"

MANUFACTURER ADVANCING ACCESS PATIENT ASSISTANCE PROGRAM (PAP)

- UNINSURED CLIENTS ENROLLED RECEIVE TRUVADA OR DESCOVY FREE OF CHARGE
  - HTTPS://WWW.GILEADADVANCINGACCESS.COM/FINANCIAL-SUPPORT/UNINSURED
- INSURED CLIENTS ENROLLED IN COST SHARING ASSISTANCE PROGRAM (CAP)RECEIVE A CO-PAY COUPON CARD TO COVER CO-PAYMENTS TO AN ANNUAL MAXIMUM THRESHOLD OF $7,200

  HTTPS://WWW.GILEADADVANCINGACCESS.COM/COPAY-COUPON-CARD
- GENERIC F/TDF (TEVA) CO-PAY CARD FOR INSURED CLIENTS WHO QUALIFY 1-800-433-4893
  - HTTPS://WWW.TEVAHIVGENERICS.COM



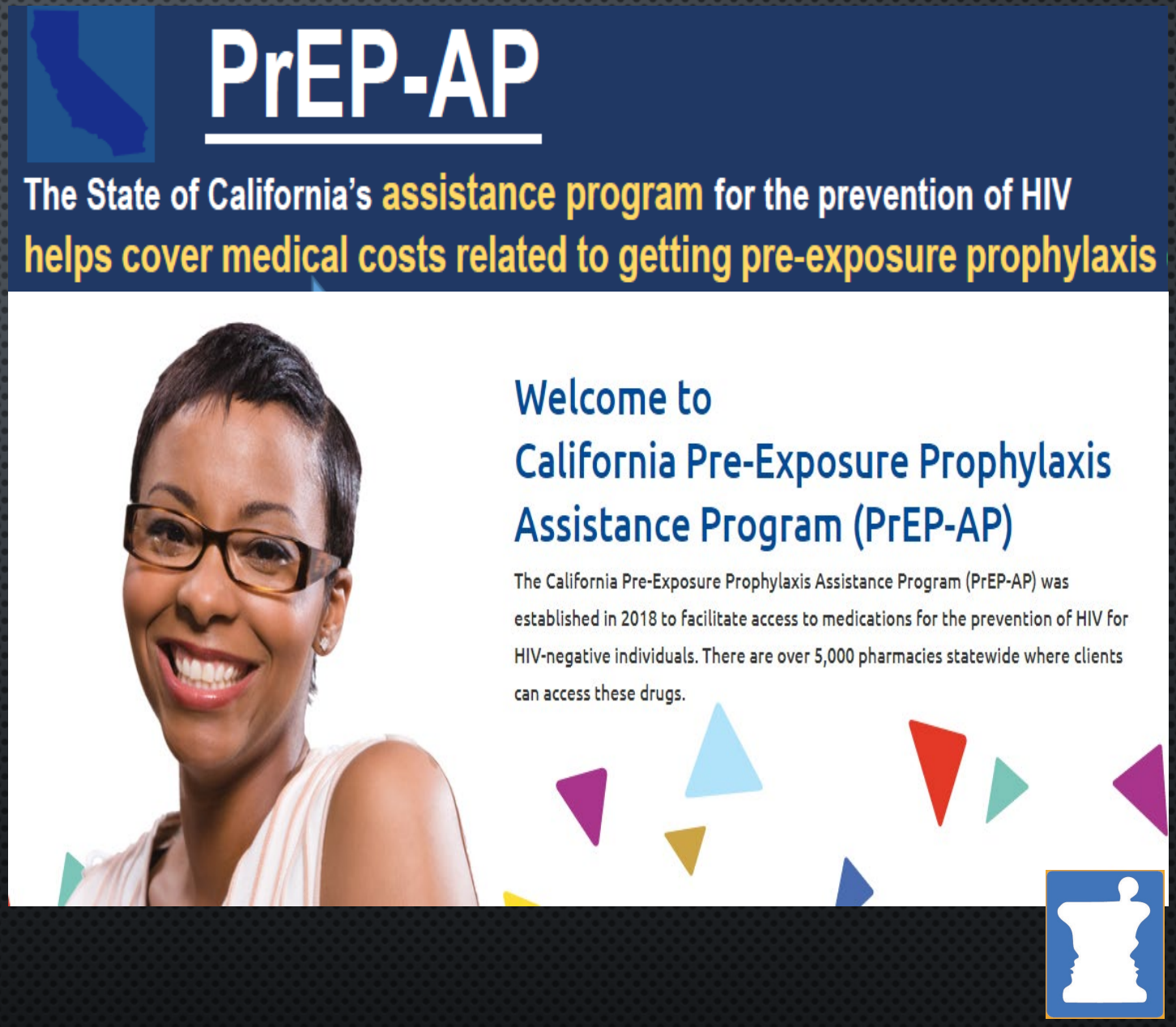
Call 1-800-226-2056

Federal Ready, Set, PrEP Program

- Visit GetYourPrEP.com or call toll-free 855-447-8410 to qualify and enroll
- PrEP coverage only
- No coverage for clinic visits or lab testing

https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/prep-program

- Provides PrEP & PEP medications, clinic visits, laboratory monitoring.
- Payer of last resort
- If not fully covered by Medical or 3rd party payers
- Provides Truvada® or Descovy® co-pays for low income insured [≤500% Federal Poverty Line (FPL)] after the $7,200 Gilead PAP benefit is exhausted



https://cdph.ca.gov

How to become a PrEP-AP provider

- Providers interested in joining the PrEP-AP Provider Network can fill out the PrEP-AP Clinical Provider Application and e-mail it to PrEPSupport@cdph.ca.gov for additional information.
- Pharmacy/pharmacist contacts CDPH/Office of AIDS (https://www.cdph.ca.gov/Programs/CID/DOA/Pages/OAadap.aspx#prep)
- Pharmacy contracts with CDPH/OA as an Enrollment Site for a defined limited enrollment service, to enroll into PrEP-AP Temporary Coverage.
- Pharmacist completes the PrEP-AP Training to enroll new clients in PrEP-AP Temporary Coverage.

https://cdph.ca.gov

PREP-AP TEMPORARY COVERAGE SUMMARY

- Pharmacist will receive payment for each client they enroll in PrEP-AP Temporary Coverage.
- PrEP-AP Temporary Coverage provides 30 days of temporary eligibility to obtain PrEP or PEP
- Clients can enroll up to two times to obtain two 30-day dispenses every two years to receive the 60-day supply per SB 159. Dispenses can be consecutive, i.e. one dispense on March 1 and return for second dispense on April 1), or 30 days supply of PEP medication

https://cdph.ca.gov

Financial Resources for PrEP and PEP

- CA PrEP-AP https://www.cdph.ca.gov
- Gilead Patient Assistant Programs (PAP) 1-800-226-2056
  https://www.gileadadvancingaccess.com/financial-support/uninsured
  https://www.gileadadvancingaccess.com/copay-coupon-card
- Federal Ready, Set, PrEP Program
  https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/prep-program
- Generic F/TDF (Teva) co-pay card for insured clients who qualify
  1-800-433-4893; https://www.tevahivgenerics.com
- Patient Advocate Foundation (PAF) 1-866-512-3861
  https://www.patientadvocate.org

PREP AND PEP CASES

LEARNING OBJECTIVES:

- APPLY KNOWLEDGE THROUGH A PREP CASE STUDY AND A PEP CASE STUDY.

LEARNING OBJECTIVES

Apply	Apply evidence-based patient counseling skills to elicit patient understanding and assess counseling needs.
Confirm	Confirm HIV status prior to starting HIV PrEP
Determine	For patients with adherence lapse, determine appropriateness of refills and HIV testing.
Utilize	Utilize appropriate patient assistance programs for uninsured patients
Link	Link patients to care for follow-up testing

PREP CASE

JP is a 20 year old cis-male who requests a refill of his PrEPand help enrolling in a Patient Assistant program. His last 30 day supply of Tenofovir DF/emtricitabine (Truvada) was 3 months ago and he has 2 refills left. He brought in his HIV negative antibody/antigen test results from 2 days ago

The pharmacists takes JP to a confidential area to discuss PrEP using language appropriate for his gender (he, him, his)

Take one minute to write down some open-ended question you would consider Asking JP before dispensing his PrEP

.

Some Assessments to Consider Before Dispensing PrEP

- Confirm HIV negative status – within 7 days before dispensing
- Be present and listen. Asses PrEP use
  - Determine adherence with daily prep? How have you been taking your prep? How do you remember to take it daily?
  - How is prep working for you? Are you having any problems or challenges with taking prep? Any questions about using prep?
  - Assess for potential drug interactions (e.g. high dose nsaids?)
  - Ask about symptoms of Acute HIV Infection and sexually transmitted diseases (STIs)
  - Inquire about any follow-up Labs: renal, HCV, sti testing
  - access to other prevention tools (i.e. condoms, sterile syringes, birth control)

Can you refill his Tenofovir DF/emtricitabine?

PREP CASE CONSULTATION

"Thank you for sharing your experience with PrEP and how it helps you. I am able to refill at least 30 days of PrEP today based on your negative HIV test result. Let's get you signed up with a Patient Assistance Program.

I have informed your provider that you requested a refill today, need a f/u appointment, your insurance has lapsed, and your HIV test 2 days ago was negative.

Inform JP a new prescription will be needed from his provider for his next Truvada refill since pharmacy has already dispensed 60 tabs

PrEP Case Summary

- Address patient using self identified gender (How would you like to be addressed?)
- Confirm HIV negative status before PrEP refills.
- Identify and Assess barriers, challenges, and support needs for gaps and nonadherence in PrEP use
- Use motivational interviewing skills and open-ended questions to engage patients for sensitive conversations
- Pharmacists can
  - enroll patients in patient assistance programs and co-pay support programs.
  - Link patients to providers for ongoing laboratory monitoring (e.g .HIV, renal function, HCV, STIs)

PEP CASE

Learning Objectives

- Assess the risk of exposure for HIV infection
- Use non-occupational post-exposure prophylaxis (nPEP) guidelines to determine appropriateness of medications.
- Counsel patients regarding appropriateness of PEP.
- Choose and dispense a appropriate nPEP regimen.
- Access patient-assistance programs as needed.
- Link patients to primary care for follow-up testing and monitoring.

PEP CASE

FL is a 55 yo transgender woman comes into your pharmacy with concerns about condom-less receptive anal intercourse approximately 24 hours ago. She knows her partner, but does not know his HIV status. She has heard that she can take a single daily tablet to reduce her risk of HIV infection. Her insurance is Medi-Cal.

Her medications include ethinyl estrogens 50 mcg daily, spironolactone 50 mg daily, metformin 850 mg TID, fluticasone-salmeterol inhaler bid and albuterol inhaler prn.

RISK ASSESSMENT

IDENTIFY THE COMPONENTS OF AN APPROPRIATE RISK ASSESSMENT:

1) IS SHE EXPOSED TO POTENTIALLY HIV INFECTIOUS BODY FLUID?
2) WAS INFECTIOUS FLUID EXPOSURE ON BODY TISSUE THAT IS SUSCEPTIBLE TO INFECTION ?
3) HOW LIKELY IS IT THAT BODY FLUID MAY CONTAIN INFECTIOUS HIV?
4) IS SHE PRESENTING FOR CARE IN TIME FOR PEP TO BE EFFECTIVE?

Infectious Body Fluids

- Semen/rectal fluids/ejaculate
- Vaginal fluids
- Blood and visible bloody body fluids
- ***Even if source person is living with HIV, body fluids are Not infectious if
  - no visible blood in Saliva, Sweat, Tears, Urine
  - Exposure onto intact skin

Likelihood of body fluid containing HIV virus

- Highest risk if living with HIV infection and not on antiretrovirals with detectable viral load (VL)
  - Persons living with HIV who achieve an undetectable VL do not transmit HIV. Undetectable = Untransmittable
- When HIV status of source is unknown, can consider risks and benefits
  - "as if person was living with HIV".
- People who are known to be negative for HIV infection carry no risk of transmission, regardless of body fluid exposure.

Timing of HIV post-exposure prophylaxis

- Starting PEP is recommended ASAP and no later than 72 hours following an exposure of infectious body fluid from a person living with HIV with a detectable viral load.
- Studies in animal models found that starting ASAP after exposure is most effective. starting PEP after 72 hours was not effective
- Starting on the day of exposure is more effective than 36 HR after exposure.
- Inappropriate to tell patients to "come back tomorrow" to start PEP.

Risk Assessment

Identify the components of an appropriate risk assessment:

1) Is she exposed to potentially HIV infectious body fluid?

   Yes, semen

2) Was infectious fluid exposure on body tissue that is susceptible to infection?

   Yes – Rectal Mucosa

3) How likely is it that body fluid may contain infectious HIV?

   Possible, HIV status unknown but obtaining a history may be helpful to ascertain risk vs. benefits of PEP

4) Is she presenting for care in time for PEP to be effective?

   Yes –within 24 hours

PEP – Selecting a Regimen

- FL prefers a single tablet for HIV protection
- All CDC recommended PEP regimens require multiple tablets
- bictegravir-tenofovir alafenamide-emtrictabine (Biktarvy®) is an effective once daily PEP regimen available on the Medi-Cal and PrEP-AP formulary.
- fewer drug interactions than protease-inhibitor regimens and dolutegravir (DTG)
  - Increased Fluticasone levels with protease inhibitor regimen
  - Increased metformin levels with DTG. metformin dose is at maximum dose and would need to be reduced if DTG started.
- Patient assistance programs (PAP) available to dispense at least 30 day of PEP
  - access one PAP if start single-tablet regimen.
  - For multiple tablet regimens, may need to contact multiple PAP.

Counseling about PEP

- Important to address FL by her self identified gender (she, her, hers)
- Identify HIV risk of her exposure.
- Reassure that starting and completing at least a 28 day course can reduce risk of HIV transmission by at least 80%
- full 28 day course needed for efficacy

transient side-effects – nausea, diarrhea, headaches, insomnia

- take with food to reduce GI effects
- Anti-emetics (i.e. ginger) to mitigate nausea
- improve with time, less with days/weeks

- check for drug interactions (e.g. Al/Mg antacids, calcium, NSAIDs)

LINKAGE TO CARE

- PATIENT APPOINTMENT WITH PROVIDER TO DO BASELINE AND FOLLOW UP TESTING: HIV, HEPATITIS B AND C, STIS, RENAL FUNCTION
- PATIENTS SHOULD BE SEEN WITHIN FIRST FEW DAYS OF STARTING HIV PEP TO ASSESS TOLERABILITY AND ADHERENCE
- PHARMACIES CAN PREPARE FOR SUCCESSFUL LINKAGE TO CARE FOR PATIENTS ON PEP BY DEVELOPING LINKAGE TO CARE PROTOCOLS WITH PROVIDERS AND CLINICS IN THEIR COMMUNITY.

Selected Resources: Linkage to Care

- Health HIV https://healthhiv.org/
- AAHIVM referral https://providers.aahivm.org/referral-link-search
- Local County Health Department https://www.cdph.ca.gov/Pages/LocalHealthServicesAndOffices.aspx#
- CDC website to find care in your area code https://www.cdc.gov
- PrEP locator: national database for US PrEP providers https://preplocator.org

Case Conclusion Summary

- Assess Risk of exposure and benefits of PEP X 28 days.
- Ensure starting PEP ASAP and < 72 hour from time of exposure.
- Access patient assistance programs if uninsured or needing copay assistance
- Counsel about transient side effects and mitigation strategies
- Link patient to care for baseline and repeat laboratory monitoring

THE END

- DIRECT QUESTIONS TO DONG.BETTY@UCSF.EDU