Implementation of HIV Prevention in Primary Care

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 - Research Support



HIV Prevention Opportunities

Patient and Behavioral Interventions USexual Partners Partner U Sharing Needles Aim: to lower the number of partners, alter risk-taking behavior **Education** Older Age at Initiation **Abstinence** of Sexual Activity **Correct &** Having only one Consistent sexual partner **Condom Use High-impact HIV Prevention** Male **Treatment** Circumcision of STIs **PEP PrEP** Treatment as **Prevention of Prevention** mother-to-child **Biomedical Interventions** (Tasp)

transmission

Aim: to reduce the efficiency of transmission or to shorten the duration of infectiousness





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- Additional, complementary prevention methods are needed.
 - That don't require use "in the moment"
 - That can be used without the cooperation or knowledge of one's partner

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- Once-daily oral tenofoviremtricitabine approved for PrEP by the FDA



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- Once-daily oral tenofoviremtricitabine approved for PrEP by the FDA
- Recommended for highrisk individuals by CDC and WHO

PrEP: Results from Clinical Trials

Clinical trial	Participants	Number	Drug	mITT ^a efficacy of % reduction in acquisition of HIV infection ^b		Adherence-adjusted efficacy based on TDF detection in blood ^c	
				%	(95% CI)	%	(95% CI)
iPrEx	Men who have sex with men (MSM)	2499	TVD	42	(15-63)	92	(40-99)
Partners PrEP	HIV discordant couples	4747	TDF	67	(44-81)	86	(67-94)
			TVD	75	(55-87)	90	(58-98)
TDF 2	Heterosexually active men and women	1200	TVD	63	(22-83)	85 ^d	NS
Bangkok Tenofovir Study	IDU	2413	TDF	49	(10-72)	74	(17-94)
Fem-PrEP	Heterosexually active women	1951	TVD	NR		NR	
VOICE	Heterosexually active women	5029	TVD	NR		NR	

- Modified Intent to Treat
- Excluded only those enrolled patients later found to be infected at randomization and those with no follow-up visit or HIV test
- The percentage of reduction in HIV incidence among those with TFV detected in blood, compared with those without detectable TFV
- d. Finding not statistically significant

US Public Health Services. Preexposure Prophylaxis For The Prevention Of HIV Infection In The United States, 2014.

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







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Vital Signs: Estimated Percentages and Numbers of Adults with Indications for Preexposure Prophylaxis to Prevent HIV Acquisition — *United States, 2015*

DAWN K. SMITH, MD; MICHELLE VAN HANDEL, MPH; RICHARD J. WOLITSKI, PHD; JO ELLEN STRYKER, PHD; H. IRENE HALL, PHD; JOSEPH PREJEAN, PHD; LINDA J. KOENIG, PHD; LINDA A. VALLEROY, PHD

25%

An estimated one in four (492,000; 95% Cl: 212,000-772,000) sexually active HIVnegative adult men who have sex with men (MSM) have Indications for PrEP consistent. with those defined in the 2014 U.S. Public Health Service preexposure prophylaxis (PrEP) clinical practice guideline.

20%

An estimated one in five (115,000: 95% Cl: 45,000-185,000) HIV-negative persons who inject drugs have Indications for PrEP.

1 in 200

An estimated one in 200 (624,000; 95% Cl: 404,000-846,000) HIV-negative heterosexually active adults have indications for PrEP.











A SCAI Center of Excellence

Steps for Clinical Implementation of PrEP

Screen for risk behaviors

HIV/STD Testing

Discuss PrEP

Initial PrEP Visit

Prescribe PrEP

Q3 Month Follow-ups









Steps for Clinical Implementation of PrEP

Screen for risk behaviors

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Prescribe PrEP

Q3 Month Follow-ups



High-Impact HIV Prevention Capacity Building Assistance for Healthcare Organizations

Short report

Retention in care outcomes for HIV pre-exposure prophylaxis implementation programmes among men who have sex with men in three US cities

Philip A Chan^{5,1}, Leandro Mena², Rupa Patel³, Catherine E Oldenburg⁴, Laura Beauchamps², Amaya G Perez-Brumer⁵, Sharon Parker⁶, Kenneth H Mayer^{7,8,9}, Matthew J Mimiaga^{7,10,11} and Amv Nunn¹¹

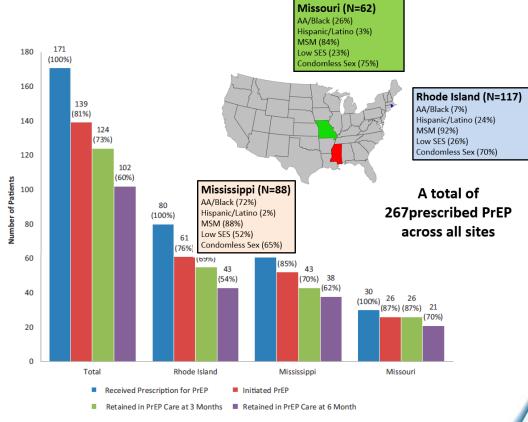
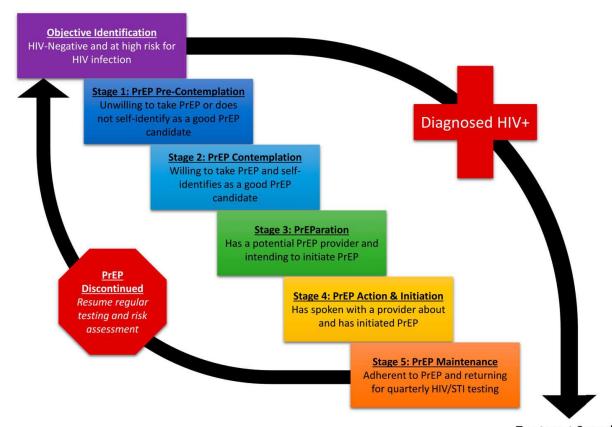


Figure 1. Retention in HIV pre-exposure prophylaxis (PrEP) care cascade overall and for Rhode Island, Mississippi and Missouri.





Motivational PrEP Cascade

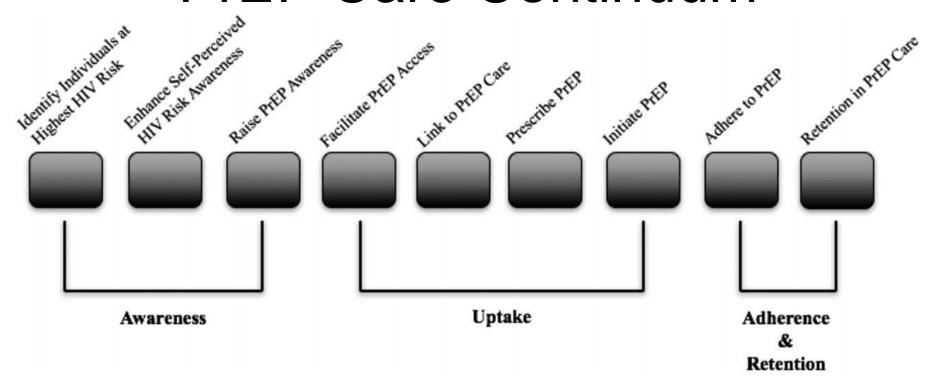


Treatment Cascade
Stage 1: HIV Diagnosis

Parsons et al., Acquir Immune Defic Syndr Volume 74, Number 3, March 1, 2017



PrEP Care Continuum

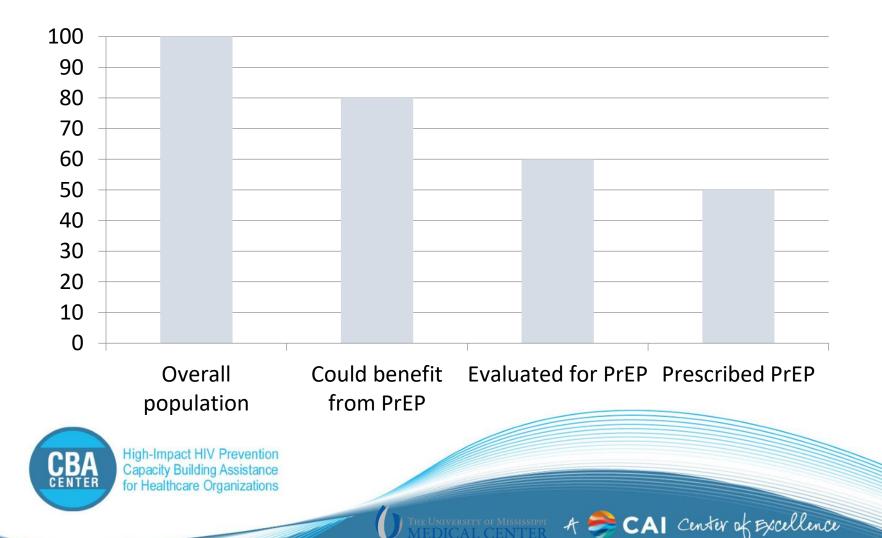




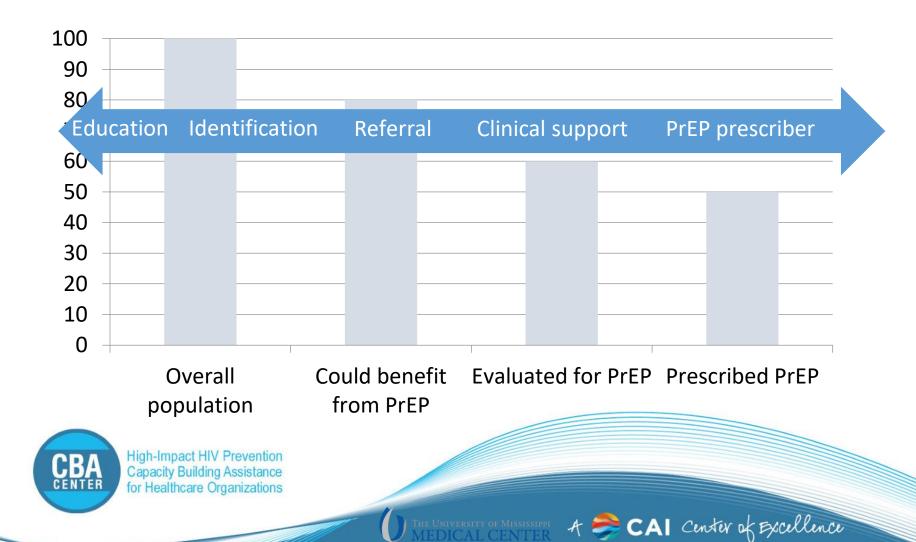
Nunn et al. AIDS 2017, 31:731-734



Potential domains of PrEP services



Potential domains of PrEP services



Case 1

- 24 year-old man referred from STI clinic
- 5 male sexual partners per month; engages in oral and anal sex; condom use inconsistent
- No chronic medical problems
- No prior sexually-transmitted infections
- Physical examination unremarkable
- HIV and STI testing one month ago was negative





Yes; according to the CDC, MSM who fulfill the following criteria are candidates







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Adult man
Without acute or established HIV infection
Any male sex partners in past 6 months

AND

Not in a monogamous partnership with a recently tested, HIV-negative man







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Adult man
Without acute or established HIV infection
Any male sex partners in past 6 months
Not in a monogamous partnership with a recently tested, HIV-negative man

AND at least one of the following

Any anal sex without condoms (receptive or insertive) in past 6 months Any STI diagnosed or reported in past 6 months Is in an ongoing sexual relationship with an HIV-positive male partner





Persons Likely to Benefit from Using PrEP

MSM and Transgender Women	Heterosexual Men and Women	Persons who Inject Drugs
Not in a monogamous relationsh partner AND/OR	ip with recently tested, HIV-neg	Any use of injection drugs AND
Ongoing relationship with HIV+ partner	Ongoing relationship with HIV + partner	Any sharing of injection equipment (past 6 months)
☐ Condomless anal sex (past 6 months)	Man who is behaviorally bisexual	☐ Been in methadone, suboxone, buprenorphine treatment program (past 6 months)
☐ STI (past 6 months)	Infrequent condom use with partner(s) at risk for HIV acquisition	☐ Risk of sexual acquisition





Which tests must be sent before starting PrEP?

- 1. HIV antibody, hepatitis B surface antibody, urinalysis
- 2. HIV antibody, hepatitis B surface antigen, serum creatinine
- 3. HIV RNA, hepatitis B surface antibody, urinalysis
- 4. HIV RNA, hepatitis B surface antigen, serum creatinine

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 Determine Eligibility (negative HIV test, at high-risk for HIV acquisition, screen/treat for STDs, screen/vaccinate for Hep B; pregnancy test) and r/o acute infection

US Public Health Service

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES - 2014













- Determine Eligibility (negative HIV test, at high-risk for HIV acquisition, screen/treat for STDs, screen/vaccinate for Hep B; pregnancy test) and r/o acute infection
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- Monitor

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV

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 - HIV status every 3 months

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US Public Health Service

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED **STATES - 2014**





CDC Guidance on Prescribing PrEP

- Determine Eligibility (negative HIV test, at high-risk for HIV acquisition, screen/treat for STDs, screen/vaccinate for Hep B; pregnancy test) and r/o acute infection
- Prescribe tenofovir-emtricitabine 1 tablet by mouth daily x 90 days
- Provide condoms, adherence and risk-reduction counseling or referral
- Monitor
 - HIV status every 3 months
 - Renal function at 3 months and every 6 months
 - Risk reduction, condoms, STI assessments /Rx

US Public Health Service

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES - 2014

A CLINICAL PRACTICE GUIDELINE







What would you tell him about side effects?

- Nausea may occur with initiation of tenofoviremtricitabine; it typically resolves with time.
- Kidney injury occurs rarely (2% in iPrex).
 - Periodic monitoring is obligatory.
 - Abnormalities usually resolve with drug discontinuation.
- A small decrease in bone mineral density may occur; the clinical significance of this is unknown.
- Antiretroviral resistance is unlikely but possible.

How would you counsel him about...

- The length of time on PrEP before he is maximally protected?
 - 7 days, when maximal levels are achieved in rectal tissue?
- If stopping PrEP, how long he should take it beyond his last high-risk sexual encounter?
 - 4 weeks, by analogy to PEP





My talking points with a new patient

- PrEP efficacy and importance of adherence
- Periodic HIV testing and creatinine checks are mandatory.
- The risk of HIV drug resistance if he/she becomes infected with HIV while on PrEP
- Side effects: GI, renal, bone
- What we think about time to maximal protection, time to continue after last high-risk encounter
- PrEP does not protect against other STIs, except perhaps HSV (Celum, Ann Intern Med, 2014).
- Let us know if they discontinue using PrEP so we can work together in an alternative safety plan



- 38 year-old man referred after diagnosis of rectal HSV; eager to start PrEP
- 1-2 new sexual encounters per month, mostly with male partners
- Physical examination unremarkable
- HIV antigen/antibody negative, HBsAg negative, creatinine 0.89 (eGFR > 60)
- Unprotected receptive anal sex 1 day ago

How would you manage his recent, high risk exposure in the context of PrEP?

- Send an HIV viral load and start PrEP if it's negative
- 2. Wait 4 weeks, then recheck an HIV antibody/antigen test and start PrEP if negative
- 3. Start PrEP now
- 4. Start post-exposure prophylaxis with tenofoviremtricitabine + dolutegravir, then continue PrEP alone after 28 days

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PEP to PrEP Transition

- PEP is a response to an acute exposure
- Some patients who present for PEP may have high risk for HIV
- When monitoring PEP, ascertain if the patient would benefit from PrEP
- It is important to confirm if the patient is HIV infected prior to transitioning from PEP to PrEP
- PEP entails taking up to 3 medications daily for 28 days; PrEP entails 1 pill/day while risk persists
 - Adherence counseling is important



Jain S, et al. Clin Infect Dis. 2015;60(suppl 3):S204.NYnPEPGuideline. 2014.



Case 2, follow-up

- He starts 3-drug PEP, then continues PrEP alone after 28 days.
- At a 3-month follow-up, his HIV test is negative, and his creatinine is stable.
- His sexual behavior is unchanged.
- He has heard that "on-demand" PrEP (that taken only in the context of sex) can also reduce HIV transmission and wants to stop daily use.

Would you...

- 1. Endorse "on-demand" (episodic) PrEP?
- 2. Recommend that he continue daily PrEP?





Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
		Х	X	X	







• **Population:** 400 MSM reporting unprotected sex with 2 or more partners in the past 6 months

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
		X	X	X	







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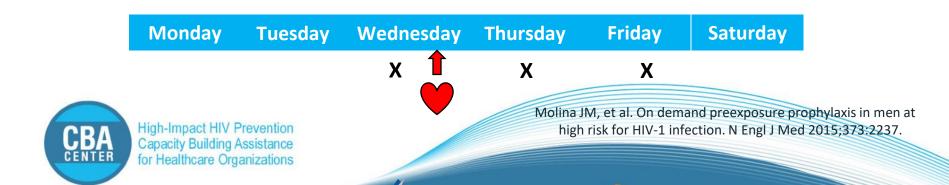
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		Х	X	X	





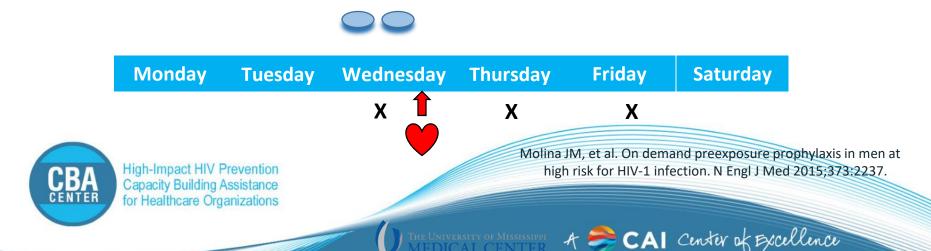


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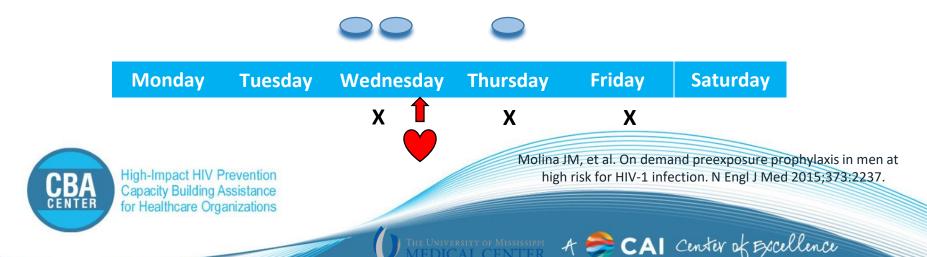


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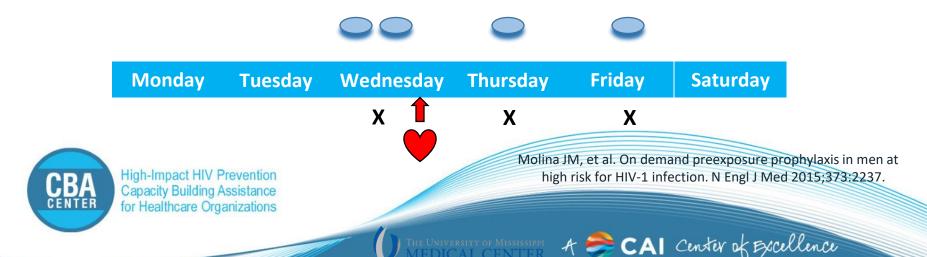
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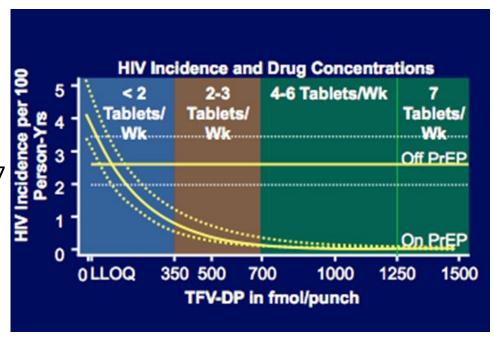
iPrEX OLE: PrEP Reduces Incidence of HIV Even with Incomplete Adherence

Open-label extension of iPrEX trial; N = 1603 (75% receiving PrEP)

100% adherence was not required to attain full benefit from PrEP

- Benefit of 4-6 tablets/wk similar to 7 tablets/wk
- 2-3 tablets/wk also associated with significant risk reduction

Higher levels of sexual risk taking at baseline associated with greater adherence to PrEP



Grant RM, et al. Lancet Infect Dis. 2014;14:820-829 Grant RM, et al. IAC 2014. Abstract TUAC0105LB

CDC still recommends daily PrEP









 A 27 year-old gay man in generally good health presents to establish care.





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- He has had a cold with fever, sore throat, and swollen glands for 2 days; taking frequent ibuprofen





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- Unprotected anal sex with 1 primary and 2 occasional male sex partners; most recently 10 days ago





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- He has had a cold with fever, sore throat, and swollen glands for 2 days; taking frequent ibuprofen
- Unprotected anal sex with 1 primary and 2 occasional male sex partners; most recently 10 days ago
- HIV antibody and HBsAg negative; creatinine normal
- Interested in PrEP





Would you...

- 1. Start PrEP
- 2. Send an HIV viral load and base the PrEP decision on the result
- 3. Wait until his cold has improved and he's stopped ibuprofen; then start PrEP
- Start PEP, then transition to PrEP after 28 days





Remember features of acute HIV

FEATURE	FREQUENCY (%)
Fever	77
Myalgia	52
Rash	51
Headache	47
Pharyngitis	43
Cervical adenopathy	41
Diarrhea	28

Daar ES, Pilcher CD, Hecht FM. Curr Opin HIV AIDS. 2008.

www.lgbthealtheducation.org







Case 3, follow up

 HIV RNA 2.5 million; antibody seroconversion within one week

Acute HIV and PrEP:

- Patients may be symptomatic from acute HIV but have negative serologic testing (i.e., in the "window period").
- In clinical trials of PrEP, drug resistance has been seen in those who were in the window period at enrollment.
- Use of the 4th-generation antibody/antigen test decreases but does not eliminate the window period.
- Send an HIV RNA if in doubt.
- Hold PrEP initiation until HIV negative status confirmed



Resistance is rare but occurs in those who are in the window period upon PrEP initiation.

TRIAL	RESISTANCE AMONG THOSE INFECTED AT ENROLLMENT	RESISTANCE AMONG THOSE INFECTED LATER IN THE STUDY
iPrex	1 of 8 in the placeboarm 2 of 2 in the PrEP arm	0 of 64 in the placeboarm 0 of 36 in the PrEP arm
Partners PrEP	0 of 6 in the placeboarm 2 of 8 in the PrEP arms	0 of 52 in the placeboarm 0 of 30 in the PrEP arms
TDF2	0 of 2 in the placeboarm 1 of 1 in the PrEP arm	1 of 24 in the placeboarm 0 of 9 in the PrEP arm
TOTAL	1 of 16 in placebo arms 5 of 11 in PrEP arms	1 of 140 in placeboarms 0 of 75 in PrEP arms

Of 7 subjects who had drug resistance, 5 were unknowingly infected with HIV when they started PrEP.





- 48 year-old man referred for PrEP
- Obesity, hypertension, sleep apnea
- Monogamous with one male partner who is HIV infected but virologically suppressed
- HIV antibody/antigen and HBsAg negative; creatinine 1.09 (eGFR > 60)
- He asks if PrEP for him is worthwhile since his partner is undetectable.

Would you recommend PrEP?

- 1. Yes
- 2. No





No Yes





No Yes

 HIV treatment prevents transmission; the additional benefit of PrEP may not outweigh its risks, however small.





No Yes

- HIV treatment prevents transmission; the additional benefit of PrEP may not outweigh its risks, however small.
- Viral rebound may occur because of poor ART adherence or other reasons.



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- People may not be monogamous.



The utility of PrEP on top of HIV treatment is unknown

No Yes

- HIV treatment prevents transmission; the additional benefit of PrEP may not outweigh its risks, however small.
- Viral rebound may occur because of poor ART adherence or other reasons.
- People may not be monogamous.
- CDC guidelines support PrEP in this context.



PrEP if Serodiscordant Partner has a Suppressed Viral Load?

	HISK	Behaviour Reported I	by the HIV Ne	gative Partner a	and Hates of Transmis	SION	
HIV status and sexual orientation of couples	Risk behaviour reported by HIV -ve partner	Number of events (linked HIV transmissions)	Couple- years of follow up (CYFU)	Estimated number of sex acts	Transmission risk per condomless sexual contact (95% CI)	Rate of within couple HIV transmission (per 100 CYFU) (95% CI)	10 year risk of within couple HIV transmission (95% CI)
Overall	Condomless sex	0	894	44,439	0 (0 - 0.00008)	0 (0-0.40)	0 (0 - 3.9%)
	Condomless sex VL<50	0	836	41,479	0 (0 - 0.00009)	0 (0-0.43)	0 (0 - 4.2%)
	Condomless anal sex	0	374	21,032	0 (0 - 0.00017)	0 (0-0.96)	0 (0 - 9.2%)
HT m+/f- partners	Condomless sex	0	288	13,728	0 (0 - 0.00028)	0 (0-1.25)	0 (0 - 11.7%)
	Condomless vaginal sex with ejaculation	0	191	8,915	0 (0 - 0.00043)	0 (0-1.88)	0 (0 - 17.1%)
	Condomless vaginal sex without ejaculation	0	174	6,377	0 (0 - 0.00060)	0 (0-2.07)	0 (0 - 18.7%)
HT m-/f+ partners	Condomless sex	0	298	14,295	0 (0 - 0.00027)	0 (0-1.21)	0 (0 - 11.4%)
	Condomless vaginal sex	0	272	14,149	0 (0 - 0.00027)	0 (0-1.32)	0 (0 - 12.4%)
MSM	Condomless anal sex	0	308	16,416	0 (0 - 0.00023)	0 (0-1.17)	0 (0 - 11.0%)
	Condomless receptive anal sex (with or without ejaculation)	0	182	7,738	0 (0 - 0.00050)	0 (0-1.97)	0 (0- 17.9%)
	Condomless insertive anal sex	0	262	11,749	0 (0 - 0.00033)	0 (0-1.37)	0 (0 - 12.8%)

Figure 1. Rate of HIV Transmission According to Sexual Behavior Reported by the HIV-negative Sexual Partner

Rodger JAMA 2016; Grulich, CROI, 2015



High-Impact HIV Prevention Capacity Building Assistance for Healthcare Organizations

PARTNER study

- 888 HIV serodiscordant couples
- HIV+ partner VL < 200
- 39% MSM couples
- Condomless sex acts: 36K heterosexual, 22K MSM
- No transmissions

Opposites Attract

- 234 HIV serodiscordant MSM couples
- Thousands of condomless anal exposures
- No HIV transmissions when HIV + partner PVL was suppressed





Case 5

- A 42-year-old transgender woman presents with rectal pain and discharge.
- She reports having multiple male sexual partners with whom she engages in receptive anal sex, often without condoms.
- Rectal NAAT testing is positive for gonorrhea; she receives ceftriaxone and azithromycin, and her symptoms resolve.
- At follow-up, you suggest she consider PrEP for HIV prevention.
- She has been using an estradiol patch for 5 years and is concerned that PrEP may interact with her hormonal therapy.

Which is true about PrEP and hormonal therapy?

- 1. Estradiol lowers the concentrations of tenofoviremtricitabine, so the dose of PrEP should be doubled.
- 2. PrEP lowers the concentrations of estrogen in the body, so her estradiol dose may need to be increased.
- 3. Use of PrEP along with hormonal therapies is contraindicated.
- There are no known drug interactions between tenofovir-emtricitabine and cross-sex hormonal treatment.

High-Impact HIV Prevention Capacity Building Assistance for Healthcare Organizations





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Case 6

- A 36 year-old woman and her 39 year-old husband present to discuss conception.
- He's HIV infected and virologically suppressed on ART; she's HIV-negative.
- They want to conceive a child and cannot afford sperm washing.
- They ask if you would recommend PrEP for her and condomless sex in this situation.

What would you say?

- 1. Yes
- 2. No





PrEP may be part of a conception strategy

- No increased birth defects with tenofovir-emtricitabine among women in the Antiretroviral Pregnancy Registry (1)
- Other reproductive strategies for such couples may be limited to non-existent.
- However, modeling suggests PrEP adds little, assuming ART and other factors are optimized (2)





- 1. Antiretroviral pregnancy registry interim report. 2014. Available from: www.apregistry.com/forms/exec-summary.pdf.
- 2. Hoffman RM, et al. Benefits of PrEP as an adjunctive method of HIV prevention during attempted conception between HIV-uninfected women and HIV-infected male partners. J Infect Dis. 2015;212(10):1534.

Billing for PrEP

A 25 yo male presents concerned about condomless anal sex with another man and request an HIV test. MD notices that the patient is also due for a well visit this visit and performs it.

MD Decides to perform a preventive medicine visit exam, spends 35 min counseling including PrEP and performs a rapid HIV test and serum creatinine. Patient has been vaccinated for HBV.

Service	ICD-10 Code
General Medical Exam (WV)	Z0000
Special screening for other specified viral disease (HIV screening)	Z1159
HIV Counseling	Z717
High Risk Sexual Behavior	Z7251



PrEP/PEP Related Billing Codes

ICD-10*	Description
Z72.5	High risk sexual behavior
Z20.82	Contact with and (suspected) exposure to other viral communicable diseases
Z20	Contact with and (suspected) exposure to communicable diseases
Z20.2	Contact with and (suspected) exposure to infections with a predominantly sexual mode of transmission
Z20.6	Contact with and (suspected) exposure to HIV
Z77.21	Contact with and (suspected) exposure to potentially hazardous body fluids
W46	Contact with hypodermic needle: "the appropriate 7th character is to be added to each from category W46" A-initial encounter, D-subsequent encounter, S-sequela
W46.0	Contact with hypodermic needle (hypodermic needle stick NOS)
W46.1	Contact with contaminated hypodermic needle



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CPT Codes for Prevention Counseling

CPT	Description
99401	Prevention Counseling (15 minutes)
99402	Prevention Counseling (30 minutes)
99403	Prevention Counseling (45 minutes)
99404	Prevention Counseling (60 minutes)







PrEP Implementation Challenges

- Assisting people to apply for and enroll in public and private insurance coverage is an essential PrEP access strategy
- There are populations who continue to be uninsured; and there is no ADAP safety net
 - Undocumented
 - Low-income people who fall into Medicaid gap or from states that did not expand medicaid
 - Eligible but not enrolled
- Cost is a challenge, but by no means the only, or even the most significant, barrier to PrEP access



Take Home Points

- Daily tenofovir-emtricitabine substantially reduces the risk of HIV infection in individuals at high risk.
- Serious side effects are rare; renal function must be monitored periodically while on PrEP.
- Before starting PrEP, test for acute HIV if there are any suggestive clinical signs or symptoms.
- There is no evidence of adverse pregnancy outcomes among women who conceive on tenofoviremtricitabine.
- Cost is a challenge, but by no means the only, or even the most significant, barrier to PrEP access

Resources:

- CDC Provider Supplement: <u>https://www.cdc.gov/hiv/pdf/PrEPProviderSupplement2014.pdf</u>
- CDC PrEP Guidelines:https://www.cdc.gov/hiv/pdf/PrEPguidelines2014.pdf
- Billing for PrEP: https://www.nastad.org/resource/billing-coding-guide-hiv-prevention
- Project Inform: http://www.projectinform.org/pdf/PrEP Flow Chart.pdf
- PrEP Facts: www.prepfacts.org
- Association of Nurses in AIDS Care: http://www.nursesinaidscare.org
- Cicatelli: http://caiglobal.co/j_cba/index.php/available-cba-services



Thank you!

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Where are you in the steps of implementation of comprehensive HIV prevention in your practice?

- 1. Routine HIV screening
- 2. Identifying PrEP candidates and Prescribing PrEP
- 3. Providing education for PrEP
- 4. Referring PrEP patients to other providers
- 5. N/A



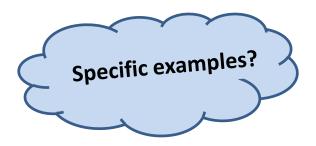


 What are the potential barriers that you may encounter when trying to implement PrEP in your practice?





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 What kind of support might you need (from your organization or others) to help you move from where you are to be able to fully integrate PrEP in your practice?





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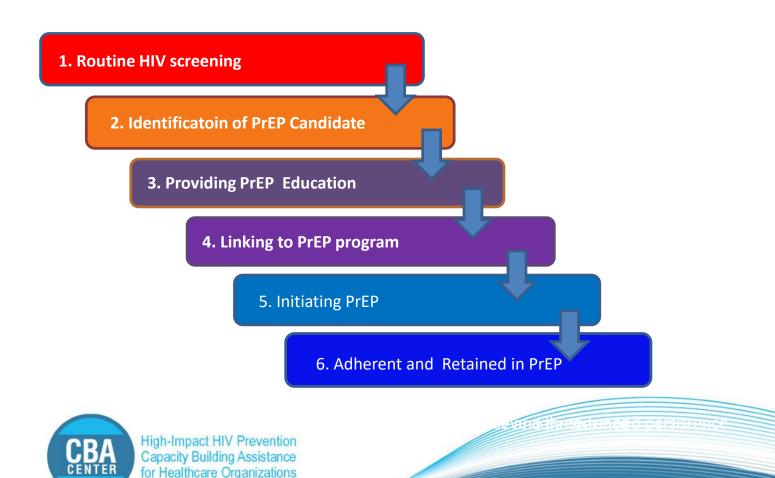
Specific examples?

 How can you improve identification of potential PrEP candidates in your practice?



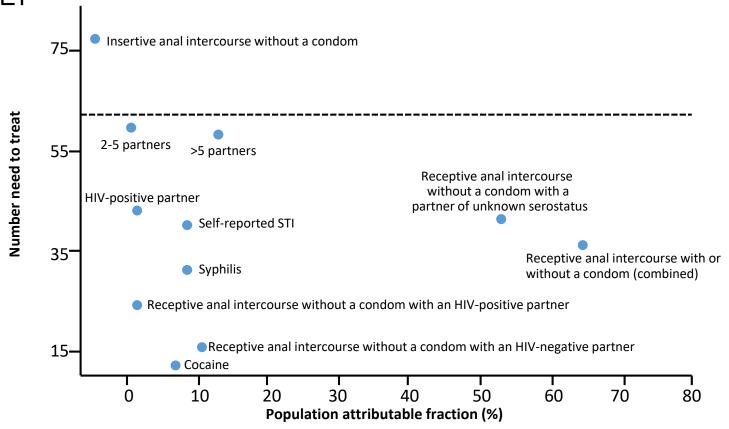


Steps for PrEP Implementation:





Quantifying Individual and Public Health Benefits of PrEP



The largest PAF was for men who had RAI without a condom, regardless of HIV status of partners (HIV+, "HIV-", or HIV-unknown).

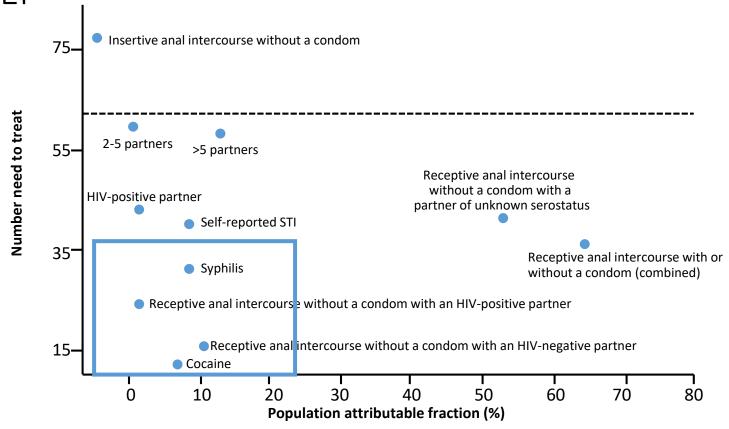
Even in this group, the number needed to treat was only 36 High-Impact HIV Prevention



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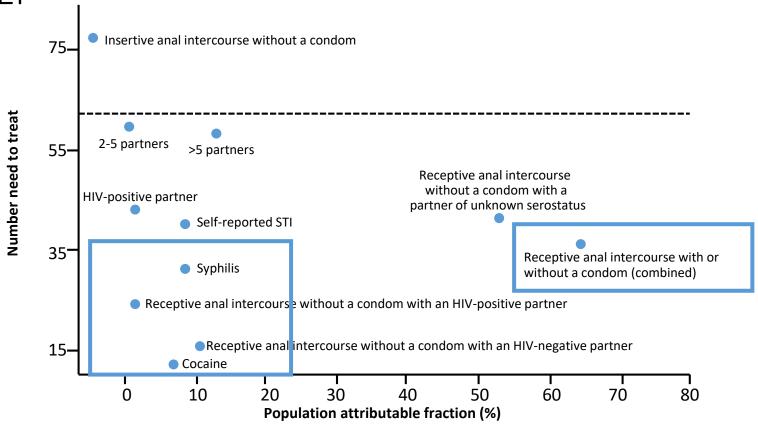
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