Implementation of HIV Prevention in Primary Care

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  - Programmatic support
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- ViiV Healthcare
  - Consulting fees
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  - Research support
- Roche Molecular Systems, Inc
  - Consulting fees
  - Research support
- Rheonix, Inc.
  - Research Support
- Thera Technologies
  - Consulting fees
  - Research Support
- Atlas Genetics Inc.
  - Research Support
HIV Prevention Opportunities

**Behavioral Interventions**
*Aim: to lower the number of partners, alter risk-taking behavior*

- Patient and Partner Education
- Abstinence
- Having only one sexual partner
- Male Circumcision
- PEP
- Treatment as Prevention (Tasp)

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

- Sexual Partners
- Sharing Needles
- Older Age at Initiation of Sexual Activity
- Correct & Consistent Condom Use
- Treatment of STIs
- PrEP
- Prevention of mother-to-child transmission

The bottom line
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• **Good but inadequate:** Condoms, abstinence, treatment of sexually-transmitted infections, male circumcision
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• **Good but inadequate**: Condoms, abstinence, treatment of sexually-transmitted infections, male circumcision

• **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
Pre-exposure prophylaxis (PrEP)

**Rationale:** Having HIV drugs present at the site of exposure should reduce the risk of infection.
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- Oral or topical antiretrovirals taken in a continuous or episodic manner
- Once-daily oral tenofovir-emtricitabine approved for PrEP by the FDA
- Recommended for high-risk individuals by CDC and WHO
# PrEP: Results from Clinical Trials

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- **a.** Modified Intent to Treat
- **b.** Excluded only those enrolled patients later found to be infected at randomization and those with no follow-up visit or HIV test
- **c.** 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

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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 (402,000; 95% CI: 212,000–772,000) sexually active HIV-negative 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% CI: 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% CI: 404,000–846,000) HIV-negative heterosexually active adults have indications for PrEP.
Steps for Clinical Implementation of PrEP

1. Screen for risk behaviors
2. HIV/STD Testing
3. Discuss PrEP
4. Initial PrEP Visit
5. Prescribe PrEP
6. Q3 Month Follow-ups
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Short report:

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

- Missouri (N=62)
  - AA/Black (26%)
  - Hispanic/Latino (3%)
  - MSM (84%)
  - Low SES (23%)
  - Condomless Sex (75%)

- Rhode Island (N=117)
  - AA/Black (7%)
  - Hispanic/Latino (24%)
  - MSM (92%)
  - Low SES (26%)
  - Condomless Sex (70%)

- Mississippi (N=88)
  - AA/Black (72%)
  - Hispanic/Latino (2%)
  - MSM (88%)
  - Low SES (52%)
  - Condomless Sex (65%)

A total of 267 prescribed PrEP across all sites.

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

Nunn et al. AIDS 2017, 31:731–734
Potential domains of PrEP services

- Overall population
- Could benefit from PrEP
- Evaluated for PrEP
- Prescribed PrEP
Potential domains of PrEP services

- Education
- Identification
- Referral
- Clinical support
- PrEP prescriber

Overall population: 100
Could benefit from PrEP: 80
Evaluated for PrEP: 70
Prescribed PrEP: 50
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
Is he a candidate for PrEP?

According to the CDC, MSM who fulfill the following criteria are candidates:

- 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

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at least one of the following

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**Persons Likely to Benefit from Using PrEP**

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<th>Heterosexual Men and Women</th>
<th>Persons who Inject Drugs</th>
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<tbody>
<tr>
<td>Not in a monogamous relationship with recently tested, HIV-neg partner AND/OR...</td>
<td>Any use of injection drugs AND...</td>
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<tr>
<td>❑ Ongoing relationship with HIV+ partner</td>
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<td>❑ Any sharing of injection equipment (past 6 months)</td>
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<tr>
<td>❑ Condomless anal sex (past 6 months)</td>
<td>❑ Man who is behaviorally bisexual</td>
<td>❑ Been in methadone, suboxone, buprenorphine treatment program (past 6 months)</td>
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<tr>
<td>❑ STI (past 6 months)</td>
<td>❑ Infrequent condom use with partner(s) at risk for HIV acquisition</td>
<td>❑ Risk of sexual acquisition</td>
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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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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
CDC Guidance on Prescribing PrEP

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• Prescribe tenofovir-emtricitabine 1 tablet by mouth daily x 90 days
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• Monitor
  • HIV status every 3 months
  • Renal function at 3 months and every 6 months
  • Risk reduction, condoms, STI assessments /Rx
What would you tell him about side effects?

- Nausea may occur with initiation of tenofovir-emtricitabine; 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
Case 2

• 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?

1. 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 tenofovir-emtricitabine + 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

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?
IPERGAY supports “on-demand” PrEP in MSM with frequent sex

- **Population:** 400 MSM reporting unprotected sex with 2 or more partners in the past 6 months
- **Intervention:** Event-driven PrEP versus placebo
- **Results:** 86% reduction in HIV incidence
- **IPERGAY regimen:** 4 pills, 3 doses over 3 days

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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

CDC still recommends daily PrEP

Case 3

• A 27-year-old gay man in generally good health presents to establish care.
• 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.
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- 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
4. Start PEP, then transition to PrEP after 28 days
Remember features of acute HIV

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<th>FEATURE</th>
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<td>77</td>
</tr>
<tr>
<td>Myalgia</td>
<td>52</td>
</tr>
<tr>
<td>Rash</td>
<td>51</td>
</tr>
<tr>
<td>Headache</td>
<td>47</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>43</td>
</tr>
<tr>
<td>Cervical adenopathy</td>
<td>41</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>28</td>
</tr>
</tbody>
</table>


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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.

<table>
<thead>
<tr>
<th>TRIAL</th>
<th>RESISTANCE AMONG THOSE INFECTED AT ENROLLMENT</th>
<th>RESISTANCE AMONG THOSE INFECTED LATER IN THE STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>iPrex</td>
<td>1 of 8 in the placebo arm</td>
<td>0 of 64 in the placebo arm</td>
</tr>
<tr>
<td></td>
<td>2 of 2 in the PrEP arm</td>
<td>0 of 36 in the PrEP arm</td>
</tr>
<tr>
<td>Partners PrEP</td>
<td>0 of 6 in the placebo arm</td>
<td>0 of 52 in the placebo arm</td>
</tr>
<tr>
<td></td>
<td>2 of 8 in the PrEP arms</td>
<td>0 of 30 in the PrEP arms</td>
</tr>
<tr>
<td>TDF2</td>
<td>0 of 2 in the placebo arm</td>
<td>1 of 24 in the placebo arm</td>
</tr>
<tr>
<td></td>
<td>1 of 1 in the PrEP arm</td>
<td>0 of 9 in the PrEP arm</td>
</tr>
<tr>
<td>TOTAL</td>
<td>1 of 16 in placebo arms</td>
<td>1 of 140 in placebo arms</td>
</tr>
<tr>
<td></td>
<td>5 of 11 in PrEP arms</td>
<td>0 of 75 in PrEP arms</td>
</tr>
</tbody>
</table>

Of 7 subjects who had drug resistance, 5 were unknowingly infected with HIV when they started PrEP.
Case 4

• 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
The utility of PrEP on top of HIV treatment is unknown

No  Yes
The utility of PrEP on top of HIV treatment is unknown

No

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

Yes
The utility of PrEP on top of HIV treatment is unknown

No

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

Yes

- Viral rebound may occur because of poor ART adherence or other reasons.
The utility of PrEP on top of HIV treatment is unknown

No

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

Yes

- Viral rebound may occur because of poor ART adherence or other reasons.
- People may not be monogamous.
The utility of PrEP on top of HIV treatment is unknown

No

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

Yes

• 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?

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

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

Rodger JAMA 2016; Grulich, CROI, 2015
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 tenofovir-emtricitabine, 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.
4. There are no known drug interactions between tenofovir-emtricitabine and cross-sex hormonal treatment.
Which is true about PrEP and hormonal therapy?

1. Estradiol lowers the concentrations of tenofovir-emtricitabine, 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.

4. There are no known drug interactions between tenofovir-emtricitabine and cross-sex hormonal treatment.
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)

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.

<table>
<thead>
<tr>
<th>Service</th>
<th>ICD-10 Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Medical Exam (WV)</td>
<td>Z0000</td>
</tr>
<tr>
<td>Special screening for other specified viral disease (HIV screening)</td>
<td>Z1159</td>
</tr>
<tr>
<td>HIV Counseling</td>
<td>Z717</td>
</tr>
<tr>
<td>High Risk Sexual Behavior</td>
<td>Z7251</td>
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</tbody>
</table>
## PrEP/PEP Related Billing Codes

<table>
<thead>
<tr>
<th>ICD-10*</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Z72.5</td>
<td>High risk sexual behavior</td>
</tr>
<tr>
<td>Z20.82</td>
<td>Contact with and (suspected) exposure to other viral communicable diseases</td>
</tr>
<tr>
<td>Z20</td>
<td>Contact with and (suspected) exposure to communicable diseases</td>
</tr>
<tr>
<td>Z20.2</td>
<td>Contact with and (suspected) exposure to infections with a predominantly sexual mode of transmission</td>
</tr>
<tr>
<td>Z20.6</td>
<td>Contact with and (suspected) exposure to HIV</td>
</tr>
<tr>
<td>Z77.21</td>
<td>Contact with and (suspected) exposure to potentially hazardous body fluids</td>
</tr>
<tr>
<td>W46</td>
<td>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</td>
</tr>
<tr>
<td>W46.0</td>
<td>Contact with hypodermic needle (hypodermic needle stick NOS)</td>
</tr>
<tr>
<td>W46.1</td>
<td>Contact with contaminated hypodermic needle</td>
</tr>
</tbody>
</table>
CPT Codes for Prevention Counseling

<table>
<thead>
<tr>
<th>CPT</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>99401</td>
<td>Prevention Counseling (15 minutes)</td>
</tr>
<tr>
<td>99402</td>
<td>Prevention Counseling (30 minutes)</td>
</tr>
<tr>
<td>99403</td>
<td>Prevention Counseling (45 minutes)</td>
</tr>
<tr>
<td>99404</td>
<td>Prevention Counseling (60 minutes)</td>
</tr>
</tbody>
</table>
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 tenofovir-emtricitabine.
• Cost is a challenge, but by no means the only, or even the most significant, barrier to PrEP access.
Resources:

- 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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Imena@umc.edu

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Discussion Questions

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
Discussion Questions

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

Specific examples?
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?
Discussion Questions

• 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?

[Specific examples?]
Discussion Questions

• How can you improve identification of potential PrEP candidates in your practice?
Steps for PrEP Implementation:

1. Routine HIV screening
2. Identification of PrEP Candidate
3. Providing PrEP Education
4. Linking to PrEP program
5. Initiating PrEP
6. Adherent and Retained in PrEP
7. Achieve adherence and persistence
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.
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