PrEP overview

Joyce Jones, MD, MS
Johns Hopkins School of Medicine
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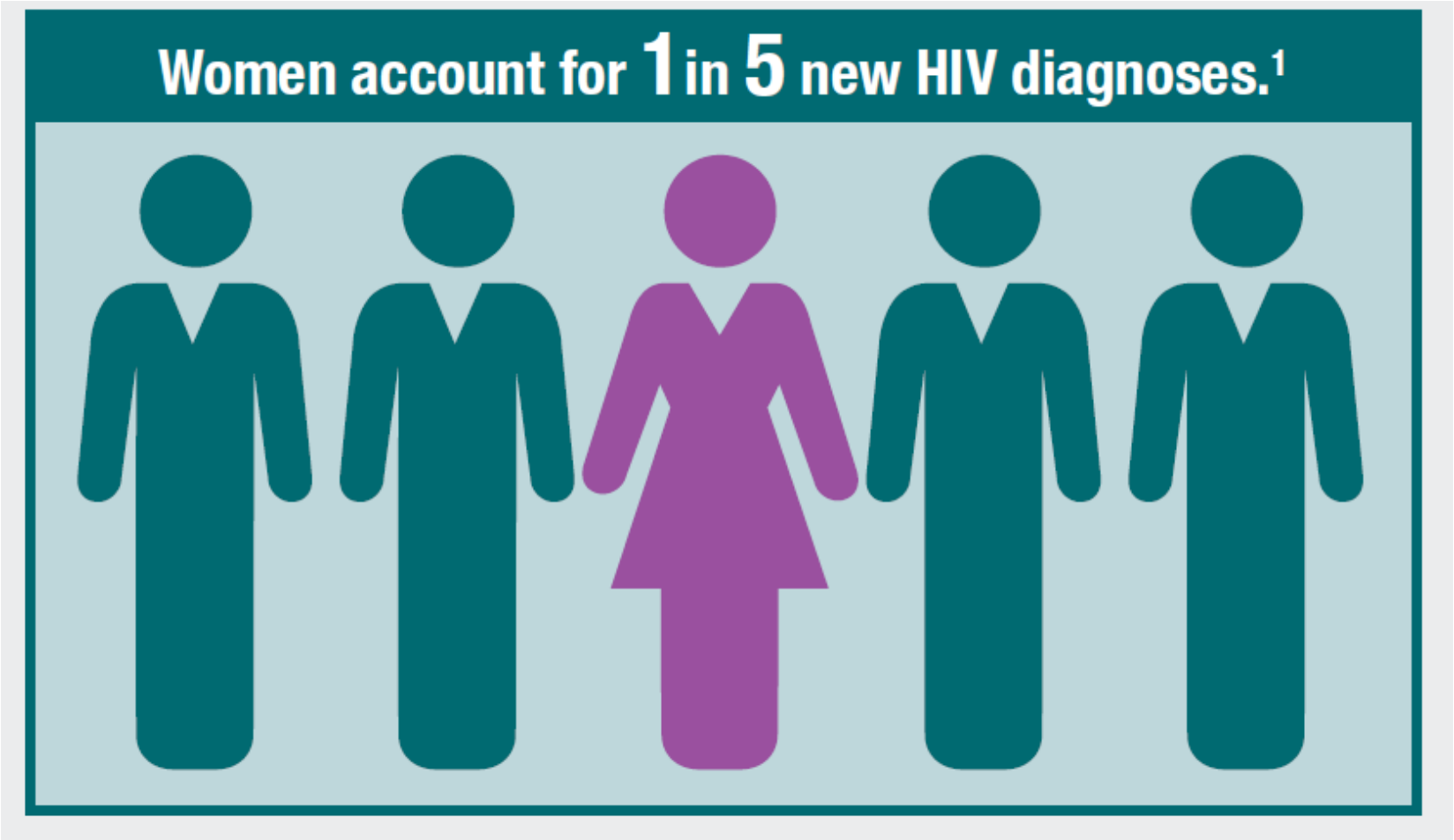
Disclosures:

None

Objectives

1. Summarize the 2017 Update of CDC clinical guidelines for PrEP
2. Highlight special considerations for PrEP and women

PrEP is for women



From https://www.cdc.gov/hiv/pdf/group/gender/women/cdc-hiv-women-and-PrEP-discussion-series.pdf, accessed 09/24/18

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What are the steps to PrEP?

1. Identify individuals at substantial risk for HIV
2. Determine clinical eligibility
3. Write a prescription
4. Provide follow up for HIV testing and other services

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Detecting substantial risk of acquiring HIV infection

Men Who Have Sex with Men	Heterosexual Women and Men	Persons Who Inject Drugs
HIV-positive sexual partner Recent bacterial STI† High number of sex partners History of inconsistent or no condom use Commercial sex work	HIV-positive sexual partner Recent bacterial STI‡ High number of sex partners History of inconsistent or no condom use Commercial sex work In high HIV prevalence area or network	HIV-positive injecting partner Sharing injection equipment

†Gonorrhea, chlamydia, syphilis for MSM including those who inject drugs
‡Gonorrhea, syphilis for heterosexual women and men including those who inject drugs

Identify individuals at substantial risk for HIV

- Perform a patient history that includes a sexual health history
- Do not limit sexual heath assessments to only selected patients
- Inform patients that brief sexual health assessments are a routine part of your practice and affirm confidentiality

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Patient assessment

- Sexual health history:
  - Gender identity
  - Sex behaviors
  - Condom use
  - Number of sex partners
  - Characteristics of sex partners
    - HIV status known/unknown
    - If HIV+ use of ART, HIV VL
    - Identity known/unknown
    - Gender identity
    - Sexual behaviors
  - History of STI
  - Symptoms of STI
  - Engagement in transactional sex
  - Last HIV test and result
  - Desire for pregnancy and contraception use
  - Use of hormones
    - Inject/share needles

Patient assessment

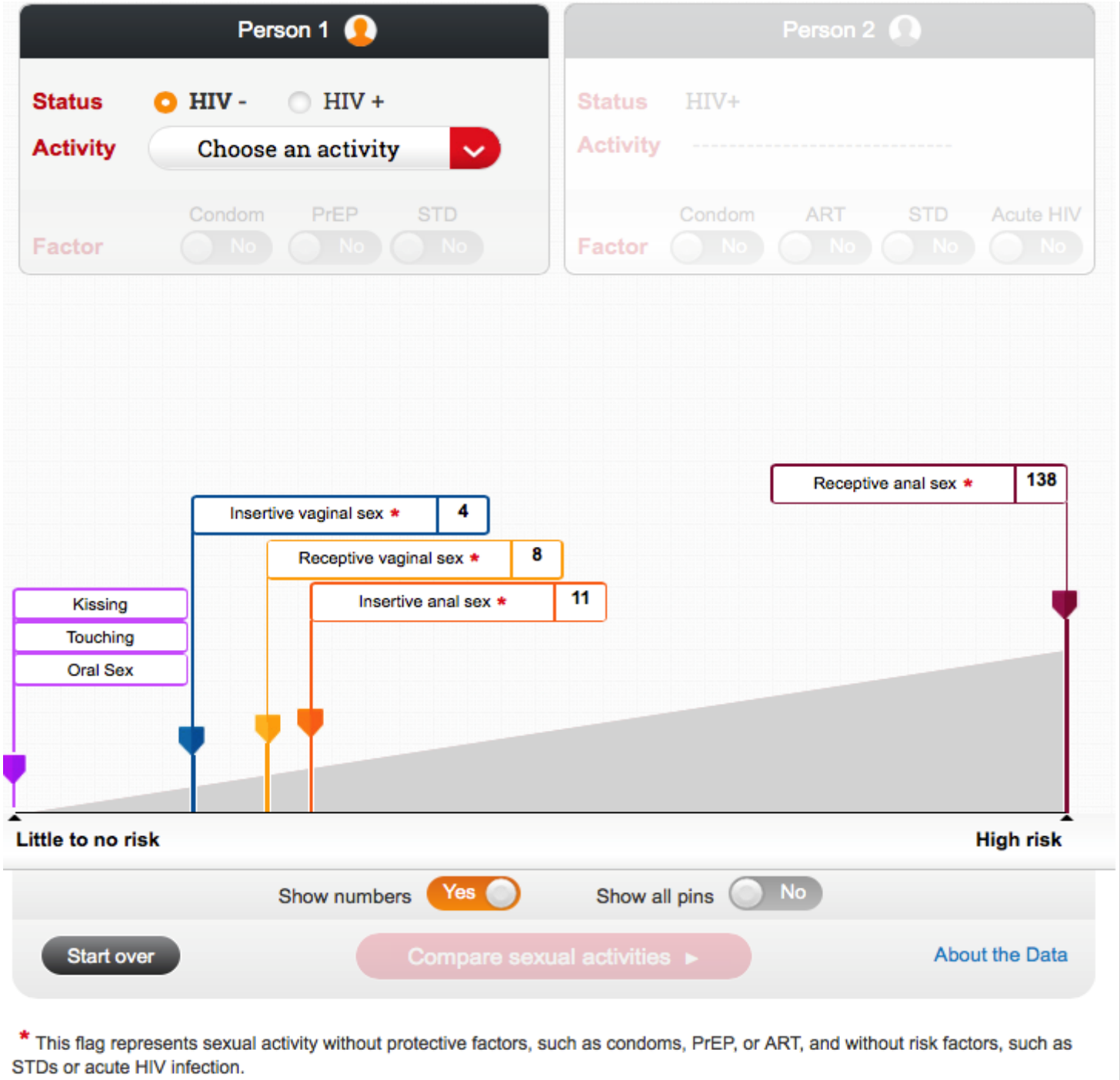
- Drug and alcohol use history
  - Sex while intoxicated
  - Frequency of use
  - Injection drug use
  - Type of drug/alcohol
  - Sharing equipment
  - Enrollment in a methadone or other medication-based drug treatment program
- Assessment of intimate partner violence
- Housing status
- Prevalence of HIV in area or network

Epidemiologic context

- http://www.cdc.gov/nchhstp/atlas/
- http://www.AIDSvu.org

CDC HIV Risk Tool

https://wwwn.cdc.gov/hivrisk/estimator.html#, accessed 09/13/18



BOX B1: RECOMMENDED INDICATIONS FOR PREP USE BY MSM[2]

- Adult man
- Without acute or established HIV infection
- Any male sex partners in past 6 months (if also has sex with women, see Box B2)
- 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
- A bacterial STI (syphilis, gonorrhea, or chlamydia) diagnosed or reported in past 6 months

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Box B2: Recommended Indications for PrEP Use by Heterosexually Active Men and Women

- Adult person
- Without acute or established HIV infection
- Any sex with opposite sex partners in past 6 months
- Not in a monogamous partnership with a recently tested HIV-negative partner

AND at least one of the following

- Is a man who has sex with both women and men (behaviorally bisexual) [also evaluate indications for PrEP use by Box B1 criteria]
- Infrequently uses condoms during sex with 1 or more partners of unknown HIV status who are known to be at substantial risk of HIV infection (PWID or bisexual male partner)
- Is in an ongoing sexual relationship with an HIV-positive partner
- A bacterial STI (syphilis, gonorrhea in women or men) diagnosed or reported in past 6 months

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Box B3: Recommended Indications for PrEP Use by Persons Who Inject Drugs

- Adult person
- Without acute or established HIV infection
- Any injection of drugs not prescribed by a clinician in past 6 months

AND at least one of the following

- Any sharing of injection or drug preparation equipment in past 6 months
- Risk of sexual acquisition (also evaluate by criteria in Box B1 or B2)

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Transgender individuals and PrEP

- Effectiveness has not been definitively proven
- Proven effectiveness to reduce risk of HIV acquisition during anal sex and penile-vaginal sex
- May be considered in all persons at risk of sexually acquiring HIV

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From the Prevention Access Campaign website,
https://www.preventionaccess.org/,
Accessed 09/18/18

Treatment as prevention and U=U considerations

- Partners with sustained viral load suppression are at no risk of sexual acquisition of HIV infection
- Must consider:
  - Recent viral load status may be unknown and/or unverifiable
  - Adherence of HIV-positive partner may be intermittent
  - HIV-negative individual may have outside partners

PrEP should not be offered as a sole intervention for HIV prevention. PrEP should only be prescribed as part of a comprehensive prevention plan.

HIV Clinical Resource. Guidance for the use of pre-exposure prophylaxis (PrEP) to prevent HIV transmission – Updated January 2014.

In addition to PrEP medication…

- Refer to drug treatment, needle exchange, mental health services, psychosocial support (housing, transportation, etc.) as indicated
- Offer gender-affirming services for transgender individuals
- Provide risk reduction counseling and condoms
- Discuss contraception options and interest in pregnancy

PrEP should be offered in supportive, non-judgmental, LGBTQ-affirming environments

PrEP and serodifferent couples

"PrEP should be discussed with heterosexually-active women and men whose partners are known to have HIV infection (i.e., HIV-discordant couples) as one of several options to protect the uninfected partner during conception and pregnancy so that an informed decision can be made in awareness of what is known and unknown about benefits and risks of PrEP for mother and fetus"

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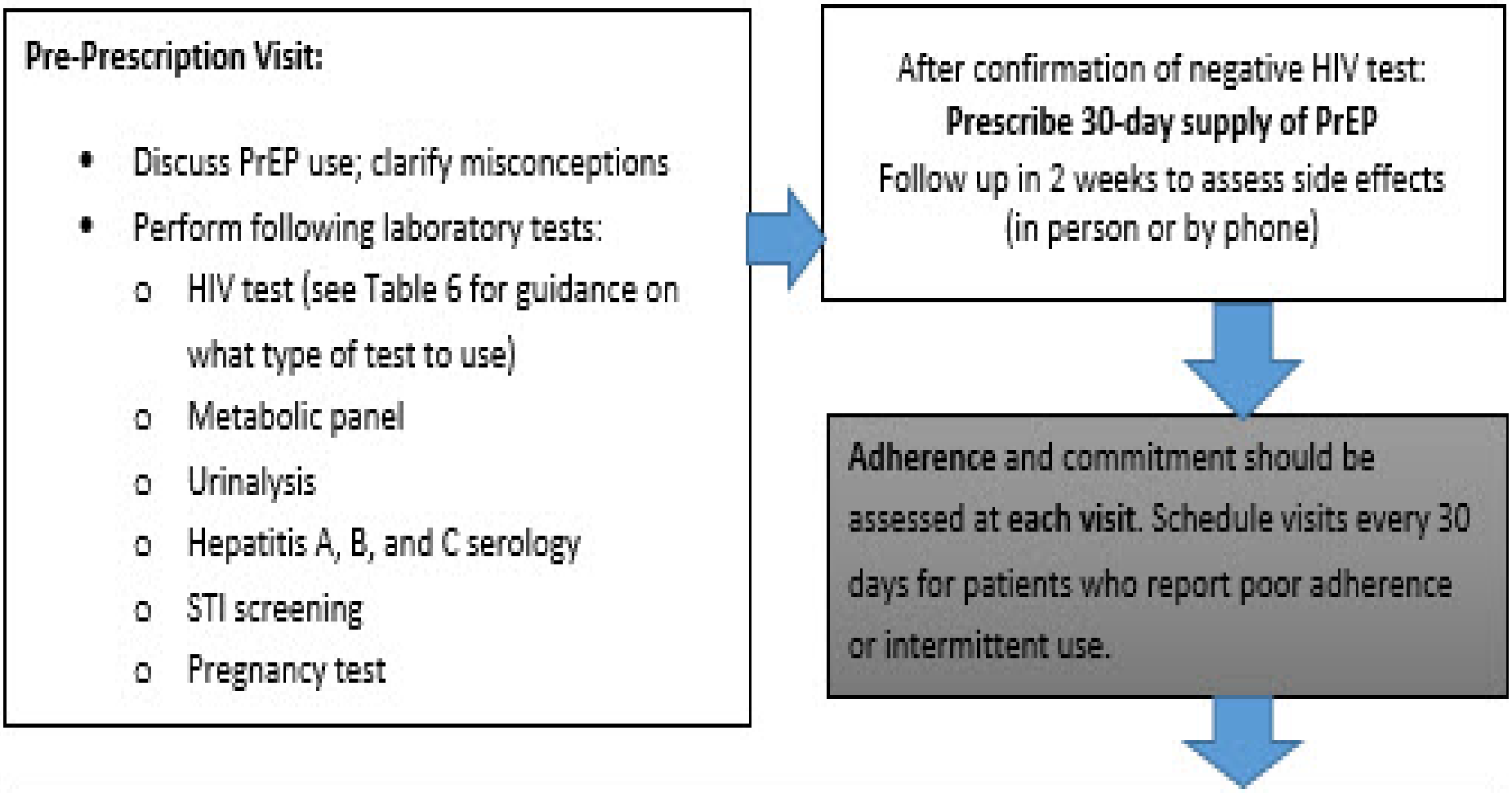
FDA expanded approval of truvada for PrEP for adolescents

- 5/15/18 expanded approval for at risk adolescents and adults ≥ 35 kg
- ATN 113 single arm, open label trial
  - N=67 young MSM 15-17 years old
  - Safe and well tolerated
  - Better adherence with more frequent visits
- Guidelines for use in adolescents will be included in next CDC update



New York State Department of Health AIDS Institute: *www.hivguidelines.org*, accessed 03/27/16

Determine clinical eligibility

1. Ensure patient is HIV negative
   - Preference for antigen/antibody HIV testing whenever possible
   - Negative test documented within a week of PrEP initiation/reinitiation
   - Rapid tests that use oral fluid should not be used to screen for HIV infection when considering PrEP use because they can be less sensitive than blood tests
   - Defer PrEP and perform additional testing if acute HIV infection is suspected
2. If HIV negative and exposure with substantial risk of HIV infection <72 hours consider nPEP
   - Transition to PrEP immediately after nPEP if on-going risk

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Table 8: Clinical Signs and Symptoms of Acute (Primary) HIV Infection[75]

Features	Overall (n = 375) %	Sex		Route of transmission	
		Male (n = 355) %	Female (n = 23) %	Sexual (n = 324) %	Injection Drug Use (n = 34) %
Fever	75	74	83	77	50
Fatigue	68	67	78	71	50
Myalgia	49	50	26	52	29
Skin rash	48	48	48	51	21
Headache	45	45	44	47	30
Pharyngitis	40	40	48	43	18
Cervical adenopathy	39	39	39	41	27
Arthralgia	30	30	26	28	26
Night sweats	28	28	22	30	27
Diarrhea	27	27	21	28	23

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Determine clinical eligibility

1. Ensure the patient is HIV negative
2. Ensure renal function is adequate (eCrCl of ≥60 ml/min using Cockroft-Gault equation)
   - Any person with an eCrCl of <60 ml/min should not be prescribed TDF/FTC for PrEP

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Conduct viral hepatitis and STI testing

- Hepatitis B: HepB sAg, HepB sAb, total HepB core antibody
  - Vaccinate if Hepatitis B non-immune
- Hepatitis C: Hepatitis C antibody
  - Consider annual testing for PWID and other persons with ongoing risk of HCV exposure
- GC/CT NAAT: see 2015 CDC STD guidelines
  - 3-site testing for MSM
  - Vaginal specimens for NAAT tests for women are preferred
  - Self-collected samples have equivalent performance to clinician-obtained samples
  - Ask about anal receptive intercourse in all individuals
- Syphilis serology: see 2015 CDC STD guidelines for recommended assays
- HPV immunization per vaccination guidelines (my recommendation, not noted in CDC guidelines)

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Patient education

- Teach how PrEP works
- Define limits of PrEP
  - Adherence
  - Lack of protection against STIs
  - Does not offer 100% protection against HIV
- Reinforce daily dosing
- Review adverse effects (nausea, headache, rash, flatulence, nephrotoxicity, decreased bone mineral density)
- Long-term safety of PrEP in HIV-seronegative individuals is unknown

Daskalakis. HIV Preexposure Prophylaxis in the real world. *Top Antivir Med.* 2014;22(4):670-675

Patient education

- Need for follow up and testing every 90 days
- Stopping criteria for PrEP
  - Positive HIV result
  - Renal disease
  - Non-adherence
  - Change in risk-taking behavior
- Symptoms of acute HIV infection
- For women:
  - How PrEP can help prevent HIV infection acquisition during pregnancy
  - Potential but undemonstrated risk of birth defects

Daskalakis. HIV Preexposure Prophylaxis in the real world. *Top Antivir Med.* 2014;22(4):670-675

PrEP and pregnancy

- A single small study of periconception use of TDF in 46 uninfected women in HIV-discordant couples found no ill effects on the pregnancy and no HIV
- TDF and FTC are widely used for the treatment of HIV infection and continued during pregnancies that occur
- The data on pregnancy outcomes in the Antiretroviral Pregnancy Registry provide no evidence of adverse effects among fetuses exposed to these medications

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PrEP and breast feeding

- The safety of PrEP with TDF/FTC or TDF alone for infants exposed during lactation has not been adequately studied.
- Data from studies of infants born to HIV-infected mothers and exposed to TDF or FTC through breast milk suggest limited drug exposure.
- World Health Organization has recommended the use of TDF/FTC or 3TC/efavirenz for all pregnant and breastfeeding women for the prevention of perinatal and postpartum mother-to-child transmission of HIV.
- Providers should discuss current evidence about the potential risks and benefits of beginning or continuing PrEP during breastfeeding so that an informed decision can be made (See Clinical Providers' Supplement, Section 5)

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PrEP and breastfeeding

"Although the DHHS Perinatal HIV Guidelines state that 'pregnancy and breastfeeding are not contraindications for PrEP,' the FDA-approved package insert says, 'If an uninfected individual becomes pregnant while taking TRUVADA for a PrEP indication, careful consideration should be given to whether use of TRUVADA should be continued, taking into account the potential increased risk for HIV-1 infection during pregnancy' and 'mothers should be instructed not to breastfeed if they are receiving TRUVADA, whether they are taking TRUVADA for treatment or to reduce the risk of acquiring HIV-1.' Therefore both are currently off-label uses of Truvada."

CDC. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2017 Update Clinical Providers' Supplement.

Prescribe PrEP

- The only medication regimen approved by the Food and Drug Administration and recommended for PrEP with all the populations specified in this guideline is daily TDF 300 mg co-formulated with FTC 200 mg (Truvada) **(IA)**

- TDF alone has shown substantial efficacy and safety in trials with PWID and heterosexually active adults and can be considered as an alternative regimen for these populations, but not for MSM, among whom its efficacy has not been studied. **(IC)**

- The use of other antiretroviral medications for PrEP, either in place of or in addition to TDF/FTC (or TDF) is not recommended. **(IIIA)**

- The prescription of oral PrEP for coitally-timed or other noncontinuous daily use is not recommended. **(IIIA)**

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DO NOT use tenofovir-alafenamide (TAF) for PrEP

Sample site	Tenofovir level (TAF vs. TDF)
Plasma	19X lower
Cervical and vaginal tissue	2X lower
Cervical and vaginal fluid	11X lower
Rectal tissue	10X lower
PBMC (TFV-DP)	9X higher (TFV-DP)

TDF = tenofovir disoproxil fumarate
TFV-DP = tenofovir diphosphate (active agent)

Less duration of detectable levels over time (TAF vs. TDF)
More research is needed to determine efficacy for PrEP

Garrett KL et al., CROI 2016.

Insurance/financial coverage of PrEP

- Ensure patient has adequate coverage for medications, lab tests, clinic visits
- Utilize local resources and pharmacy assistance programs (Gilead)

Time to achieve protection

- The time from initiation of daily oral doses of TDF/FTC to maximal protection against HIV infection is unknown.

- There is not scientific consensus on what intracellular concentrations are protective for either drug or the protective contribution of each drug in specific body tissues. It has been shown that the pharmacokinetics of TDF and FTC vary by tissue

- Exploratory data suggest maximum intracellular concentrations of tenofovir are reached:
  - in blood after approximately 20 days
  - in rectal tissue at approximately 7 days
  - in cervicovaginal tissues at approximately 20 days
  - No data are yet available about intracellular drug concentrations in penile tissues to inform time to protection for male insertive sex partners

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Clinical follow up

- **At least every 3 months to**
  - Repeat HIV testing and assess for signs or symptoms of acute infection to document that patients are still HIV negative (see Figure)
  - Repeat pregnancy testing for women who may become pregnant
  - Provide a prescription or refill authorization of daily TDF/FTC for no more than 90 days (until the next HIV test)
  - Assess side effects, adherence, and HIV acquisition risk behaviors
  - Provide support for medication adherence and risk-reduction behaviors
  - Respond to new questions and provide any new information about PrEP use
  - Conduct STI testing for sexually active persons with signs or symptoms of infection and screening for asymptomatic MSM at high risk for recurrent bacterial STIs (e.g., those with syphilis, gonorrhea, or chlamydia at prior visits or multiple sex partners)

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Clinical follow up

- **At least every 6 months to**
  - Monitor eCrCl
    - If other threats to renal safety are present (e.g., hypertension, diabetes), renal function may require more frequent monitoring or may need to include additional tests (e.g., urinalysis for proteinuria)
    - A rise in serum creatinine is not a reason to withhold treatment if eCrCl remains ≥60 ml/min.
    - If eCrCl is declining steadily (but still ≥60 ml/min), consultation with a nephrologist or other evaluation of possible threats to renal health may be indicated.
  - Conduct STI screening for sexually active adolescents and adults (i.e., syphilis and gonorrhea for both men and women, chlamydia for MSM) even if asymptomatic

- **At least every 12 months to**
  - Evaluate the need to continue PrEP as a component of HIV prevention

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Future directions

- Alternate dosing intervals (i.e. on-demand PrEP)
- Alternate antiretrovirals
- Long-acting injectable antiretrovirals
- Broadly neutralizing antibodies
- Vaginal rings
- Vaginal and rectal gels
- Vaginal films
- Post-exposure prophylaxis for bacterial STI

Take home points

- PrEP works!
- CDC guidelines provide a useful template for evaluation, prescription and follow up of PrEP
- Research is on-going to increase options for PrEP and minimize risk

Thank you!

Joyce Jones
jjone154@jhmi.edu