BONUS DIGITAL CONTENT

U.S. Preventive Services Task Force

Preexposure Prophylaxis for the Prevention of HIV Infection: Recommendation Statement

Summary of Recommendation and Evidence

The USPSTF recommends that clinicians offer preexposure prophylaxis (PrEP) with effective antiretroviral therapy to persons who are at high risk of HIV acquisition *(Table 1)*. **A recommendation.**

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

Rationale

IMPORTANCE

An estimated 1.1 million individuals in the United States are currently living with HIV,[1] and more than 700,000 persons have died of AIDS since the first cases were reported in 1981.[2] In 2017, there were 38,281 new diagnoses of HIV infection reported in the United States; 81% (30,870) of these new diagnoses were among males and 19% (7,312) were among females.[2] Although treatable, HIV infection has no cure and has significant health consequences.

See related USPSTF recommendation statement at https://www.aafp.org/afp/2019/1115/od2.html and Putting Prevention into Practice on page 637.

As published by the USPSTF.

This summary is one in a series excerpted from the Recommendation Statements released by the USPSTF. These statements address preventive health services for use in primary care clinical settings, including screening tests, counseling, and preventive medications.

The complete version of this statement, including supporting scientific evidence, evidence tables, grading system, members of the USPSTF at the time this recommendation was finalized, and references, is available on the USPSTF website at https://www.uspreventiveservicestaskforce.org/.

This series is coordinated by Kenny Lin, MD, MPH, deputy editor.

A collection of USPSTF recommendation statements published in *AFP* is available at https://www.aafp.org/afp/uspstf.

IDENTIFICATION OF RISK STATUS

Although the USPSTF found inadequate evidence that specific risk assessment tools can accurately identify persons at high risk of HIV acquisition, it found adequate epidemiologic data on risk factors that can be used to identify persons at high risk of acquiring HIV infection.

BENEFITS OF PREVENTIVE MEDICATION

The USPSTF found convincing evidence that PrEP is of substantial benefit for decreasing the risk of HIV infection in persons at high risk of HIV infection, either via sexual acquisition or through injection drug use. The USPSTF also found convincing evidence that adherence to PrEP is highly correlated with its efficacy in preventing the acquisition of HIV infection.

HARMS OF PREVENTIVE MEDICATION

The USPSTF found adequate evidence that PrEP is associated with small harms, including kidney and gastrointestinal adverse effects.

U.S. PREVENTIVE SERVICES TASK FORCE ASSESSMENT

The USPSTF concludes with high certainty that the net benefit of the use of PrEP to reduce the risk of acquisition of HIV infection in persons at high risk of HIV infection is substantial.

Clinical Considerations

PATIENT POPULATION UNDER CONSIDERATION

This recommendation applies to persons who are not infected with HIV and are at high risk of HIV infection.

ASSESSMENT OF RISK

Although the USPSTF found no well-validated, accurate tools to assess risk of HIV acquisition, epidemiologic data, Centers for Disease Control and Prevention (CDC) guidelines,[3] and enrollment criteria for clinical trials provide guidance

on detecting persons who may be at high risk. Persons at risk of HIV infection include men who have sex with men, persons at risk via heterosexual contact, and persons who inject drugs. Within these groups, certain risk factors or behaviors (outlined below) can place persons at high risk of HIV infection.

It is important to note that men who have sex with men and heterosexually active persons are not considered to be at high risk if they are in a mutually monogamous relationship with a partner who has recently tested negative for HIV. In addition, all persons being considered for PrEP must have a recently documented negative HIV test result.

The USPSTF recommends that the following persons be considered for PrEP:

1. Men who have sex with men, are sexually active, and have 1 of the following characteristics:
   - A serodiscordant sex partner (i.e., in a sexual relationship with a partner living with HIV)
   - Inconsistent use of condoms during receptive or insertive anal sex
   - A sexually transmitted infection (STI) with syphilis, gonorrhea, or chlamydia within the past 6 months
2. Heterosexually active women and men who have 1 of the following characteristics:

TABLE 1

Preexposure Prophylaxis for the Prevention of HIV Infection: Clinical Summary of the USPSTF Recommendation

Population	Persons at high risk of HIV acquisition
Recommendation	Offer PrEP Grade: A
Risk assessment	Persons at risk of HIV infection include men who have sex with men, persons at risk via heterosexual contact, and persons who inject drugs. Within these groups, certain risk factors or behaviors (outlined below) can place persons at high risk of HIV infection. Men who have sex with men, are sexually active, and have 1 of the following characteristics: • A serodiscordant sex partner (i.e., in a sexual relationship with a partner living with HIV) • Inconsistent use of condoms during receptive or insertive anal sex • A sexually transmitted infection with syphilis, gonorrhea, or chlamydia within the past 6 months Heterosexually active women and men who have 1 of the following characteristics: • A serodiscordant sex partner (i.e., in a sexual relationship with a partner living with HIV) • Inconsistent use of condoms during sex with a partner whose HIV status is unknown and who is at high risk (e.g., a person who injects drugs or a man who has sex with men and women) • A sexually transmitted infection with syphilis or gonorrhea within the past 6 months Persons who inject drugs and have 1 of the following characteristics: • Shared use of drug injection equipment • Risk of sexual acquisition of HIV (see above) Persons who engage in transactional sex, persons who are trafficked for sex work, men who have sex with men and women, and transgender women and men who are sexually active can be at high risk of HIV infection and should be considered for PrEP based on the criteria outlined above.
Preventive medication	Once-daily oral treatment with combined tenofovir disoproxil fumarate and emtricitabine is the only formulation of PrEP currently approved by the U.S. Food and Drug Administration for use in the United States in persons at risk of sexual acquisition of HIV infection.
Other relevant USPSTF recommendations	The USPSTF has issued recommendations on behavioral counseling to reduce risk of sexually transmitted infections and on screening for HIV infection.

Note: For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, go to https://www.uspreventiveservicestaskforce.org/.

PrEP = preexposure prophylaxis; USPSTF = U.S. Preventive Services Task Force.

- A serodiscordant sex partner (i.e., in a sexual relationship with a partner living with HIV)
- Inconsistent use of condoms during sex with a partner whose HIV status is unknown and who is at high risk (e.g., a person who injects drugs or a man who has sex with men and women)
- An STI with syphilis or gonorrhea within the past 6 months

3. Persons who inject drugs and have 1 of the following characteristics:
   - Shared use of drug-injection equipment
   - Risk of sexual acquisition of HIV (see above)

Persons who engage in transactional sex, such as sex for money, drugs, or housing, including commercial sex workers or persons trafficked for sex work, constitute another group at high risk of HIV acquisition and should be considered for PrEP based on the criteria outlined above. Men who have sex with men and women are at risk of HIV acquisition and should be evaluated for PrEP according to the criteria outlined above for men who have sex with men and heterosexually active men.

Transgender women and men who are sexually active may be at increased risk of HIV acquisition and should be considered for PrEP based on the criteria outlined above. Transgender women are at especially high risk of HIV acquisition. The CDC estimates that approximately one-fourth of transgender women are living with HIV, and more than half (an estimated 56%) of black/African American transgender women are living with HIV.[4] Although trials of PrEP enrolled few transgender women and no trials have been conducted among transgender men, PrEP has been shown to reduce the risk of HIV acquisition during receptive and insertive anal and vaginal sex. Therefore, its use may be considered in all persons (cisgender and transgender) at high risk of sexual acquisition of HIV.

Consistent use of condoms decreases risk of HIV acquisition by approximately 80%[5] and also decreases the risk of other STIs. However, sexually active adults often use condoms inconsistently.[6] PrEP should be considered as an option to reduce the risk of HIV acquisition in persons who use condoms inconsistently, while continuing to encourage and support consistent condom use.

To date, in 3 studies, transmission of HIV to a seronegative partner from a partner living with HIV has not been observed when the seropositive partner was being treated with antiretroviral therapy and had a suppressed viral load.[7-9] It is not known whether PrEP use further decreases the risk of HIV transmission when a seropositive partner has a documented undetectable viral load.

The risk of acquisition of HIV infection is on a continuum. This risk depends on the likelihood that a specific act or activity will transmit HIV and the likelihood that a sex partner or drug-injection partner is living with HIV. The likelihood of HIV transmission is highest with needle-sharing injection-drug use and condomless receptive anal intercourse, whereas condomless insertive anal sex and condomless receptive and insertive penile-vaginal sex have a risk of transmission that is approximately 10- to 15-fold lower than receptive anal intercourse.[5] One recent study estimated the prevalence of HIV (i.e., the likelihood that a partner whose HIV status is unknown is living with HIV) as 12.4% among men who have sex with men and 1.9% among persons who inject drugs,[10] although an earlier systematic review estimated the prevalence of HIV among persons who inject drugs to be much higher (16%).[11] The prevalence of HIV among men who have sex with men and women is estimated to be intermediate between that of men who have sex with men and heterosexually active men.[12] Thus, persons at high risk of HIV acquisition via penile-vaginal intercourse, including those with a recent bacterial STI acquired via penile-vaginal intercourse, will generally be at lower absolute risk than persons at high risk via receptive anal intercourse or injection-drug use. These are factors that clinicians and patients can consider as they discuss the use of PrEP for HIV prevention.

In addition, risk behaviors should be interpreted in the context of the HIV prevalence in a community or network; that is, risk behaviors in a high-prevalence setting carry a higher risk of acquiring HIV infection than the same behaviors in a low-prevalence setting. The threshold of HIV prevalence below which PrEP has insignificant net benefit is not known.

PREVENTIVE MEDICATION

Once-daily oral treatment with combined tenofovir disoproxil fumarate and emtricitabine is the only formulation of PrEP approved by the U.S. Food and Drug Administration for use in the United States in persons at risk of sexual acquisition of HIV infection. However, several studies

reviewed by the USPSTF found that tenofovir disoproxil fumarate alone was also effective as PrEP, and CDC guidelines note that, given these trial data, tenofovir disoproxil fumarate alone can be considered as an alternative regimen for high-risk heterosexually active men and women and persons who inject drugs.[3]

According to its product label, tenofovir disoproxil fumarate/emtricitabine may be considered for use as PrEP during pregnancy.[13] No trials of oral PrEP included pregnant women; however, pregnancy is associated with an increased risk of HIV acquisition.[14] CDC guidelines recommend shared decision-making for pregnant women who are considering starting or continuing PrEP during pregnancy.

Adolescents at high risk of HIV acquisition could benefit from PrEP, and tenofovir disoproxil fumarate/emtricitabine is approved by the U.S. Food and Drug Administration for use as PrEP in adolescents who weigh at least 35 kg.[13] In addition, young men who have sex with men are at particularly high risk of HIV acquisition.[15] However, no randomized clinical trials of PrEP enrolled adolescents. Limited data suggest that PrEP use is not associated with significant adverse events in adolescents but may be associated with slightly less bone mineral accrual than would be expected.[16] The USPSTF suggests that clinicians weigh all these factors when considering PrEP use in adolescents at high risk of HIV acquisition. In addition, clinicians need to be aware of any local laws and regulations that may apply when providing PrEP to an adolescent minor.

ADDITIONAL APPROACHES TO PREVENTION

Several additional approaches for decreasing risk of HIV acquisition are also available. Consistent use of condoms decreases risk of HIV acquisition by approximately 80%[5] and reduces the risk of other STIs. The USPSTF recommends intensive behavioral counseling to reduce behaviors associated with increased risk of STIs and HIV acquisition and to increase condom use among adolescents and adults at increased risk of STIs.[17] The CDC has made several recommendations, including abstinence, reducing one's number of sex partners, and consistent condom use, to decrease risk of STIs, including HIV.[18] The CDC also recommends syringe service programs (i.e., needle exchange programs) to reduce the risk of HIV acquisition and transmission among persons who inject drugs.[19] The Community Preventive Services Task Force has also issued several recommendations on the prevention of HIV and other STIs.[20] Postexposure prophylaxis, started as soon as possible after a possible exposure event, can also decrease the risk of HIV infection.

Screening for HIV infection to detect undiagnosed cases and antiretroviral treatment in persons living with HIV to suppress viral load are both important approaches to decreasing the risk of HIV transmission at the population level, while also benefiting the individual living with HIV. The USPSTF recommends screening for HIV infection in adolescents and adults aged 15 to 65 years, younger adolescents and older adults at increased risk, and all pregnant persons.[21]

USEFUL RESOURCES

The CDC guidelines on PrEP for the prevention of HIV infection are available at https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf[3] and https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-provider-supplement-2017.pdf.[22] Additional CDC resources on PrEP for both clinicians and consumers are available at https://www.cdc.gov/hiv/risk/prep/index.html.[23] Community-level HIV prevalence data for the United States are available at https://www.cdc.gov/nchhstp/atlas.[24] The USPSTF has issued recommendations on behavioral counseling to reduce risk of STIs[17] and on screening for HIV infection.[21]

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The "Other Considerations," "Discussion," and "Recommendations of Others" sections of this recommendation statement are available at https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/prevention-of-human-immunodeficiency-virus-hiv-infection-pre-exposure-prophylaxis.

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